
Drug Action

Introduction to Pharmacology

Ron Robertson

I. Pain Relievers

A. OTC

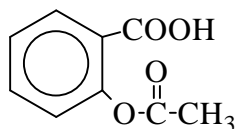
1. 1989 -- \$2.5 billion

43% aspirin

37% acetaminophen

20% ibuprofen

2. Aspirin -- Acetylsalicylic acid (1900)



a. Analgesic - pain reliever

Antipyretic - fever reducer

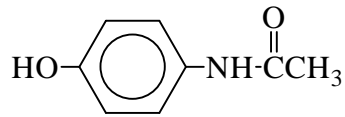
Anti-inflammatory agent - joint inflammation (high concentrations) (NSAID)

b. Inhibits the production of prostaglandins through COX-1 and COX-2 inhibition (cyclooxygenases)

c. Attacks the phospholipid lining of the stomach and can cause bleeding

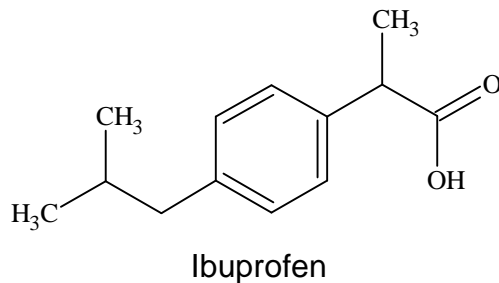
d. Helps to prevent blood clots

3. Acetaminophen (1955)



- a. Analgesic and antipyretic, not effective against arthritis. Inhibits COX-3 enzyme.
- b. Not as irritating to the stomach as aspirin

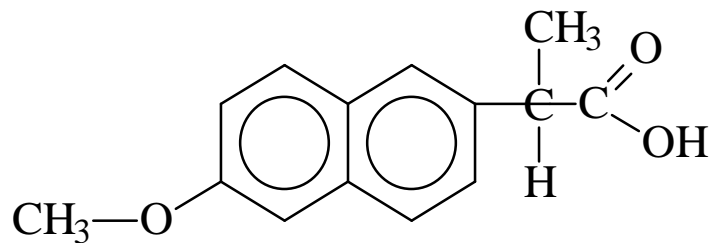
4. Ibuprofen (1983) (Motrin, Advil)



- a. Analgesic, antipyretic, anti-inflammatory agent (NSAID)
- b. More effective against soft tissue pain (higher dosage response curve)
- c. Irritating to the stomach

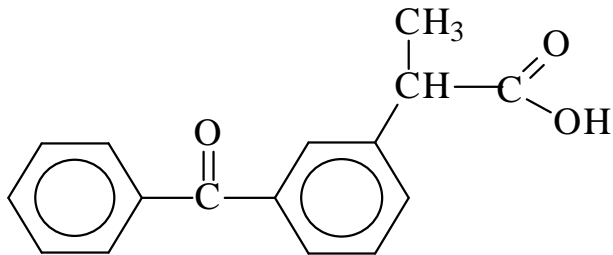
5. Naproxen (1994) (Aleve)

- a. Similar action to aspirin and ibuprofen - a nonsteroidal anti-inflammatory drug (NSAID) - thus has same advantages and disadvantages
- b. More expensive since still under patent, generic not available, only marketed under brand name
- c. Main advantage is that it needs to be taken every 8-12 hours, as opposed to 4-6 for other analgesics.



6. Ketoprofen (Orudis) (1995?)

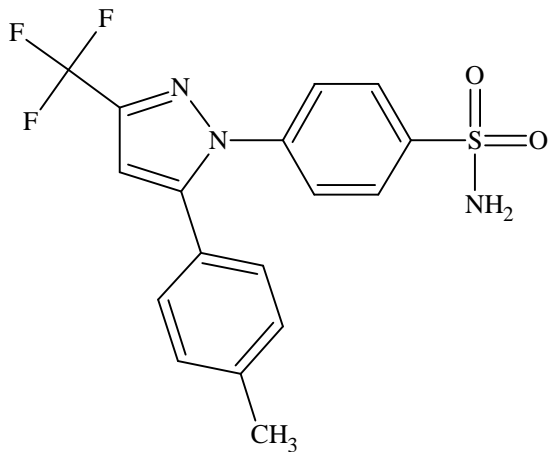
a. another NSAID



New anti-inflammatory arthritis drugs

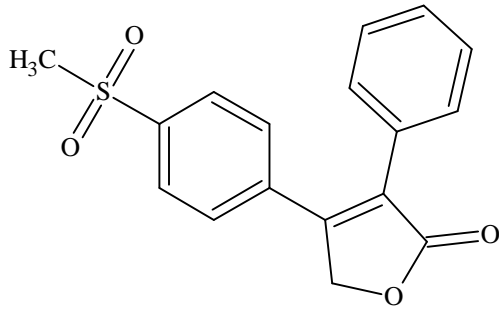
inhibit the COX-2 enzyme only

a. Celecoxib (Celebrex)



Celecoxib [Searle]

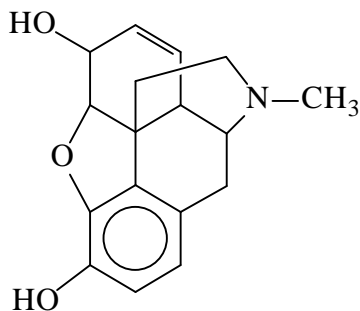
b. Rofecoxib (Vioxx)



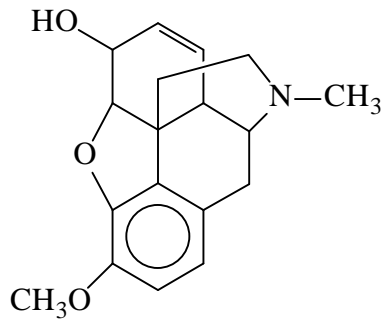
Rofecoxib [Merck & Co.]

B. Prescription Analgesics

1. Narcotic analgesic - analgesic and a sedative
2. Opiates - natural or synthetic drug which produces effects similar to morphine - derived from the opium plant
3. Opium plant derivatives - addictive
 - a. morphine



b. codeine

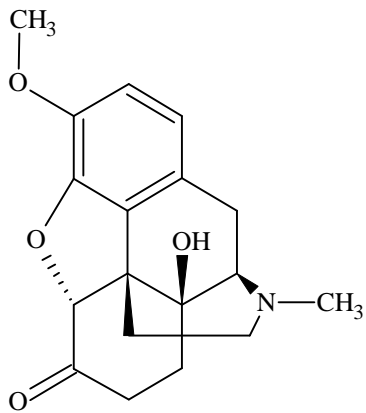


salts of these drugs are administered to increase solubility

codeine is less potent but is also less addictive

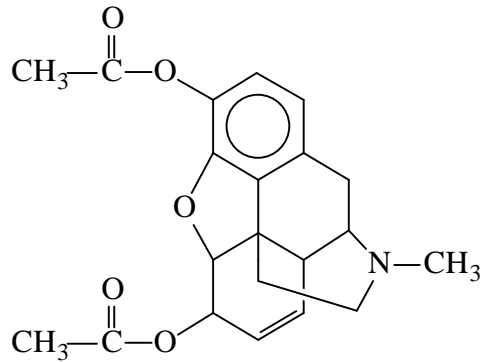
4. synthetics

a. oxycodone (Percodan)

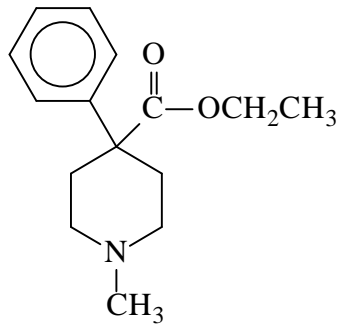


Oxycodone

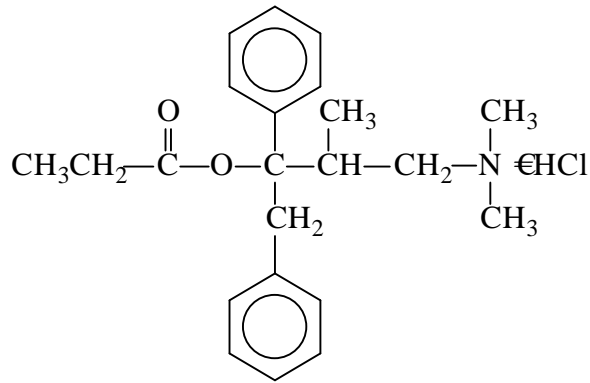
b. heroin is also a synthetic derivative and is very addictive!



b. meperidine (Demerol) --effects between codeine and morphine



c. propoxyphene (Darvon) -- effects are less than codeine



**aspirin < propoxyphene < codeine <
meperidine < morphine < heroin**

***Endorphins are peptides produced by the pituitary gland which give an analgesic effect – produced by extended physical activity like running, as well as sexual activity, childbirth, and consuming certain foods such as chocolate.

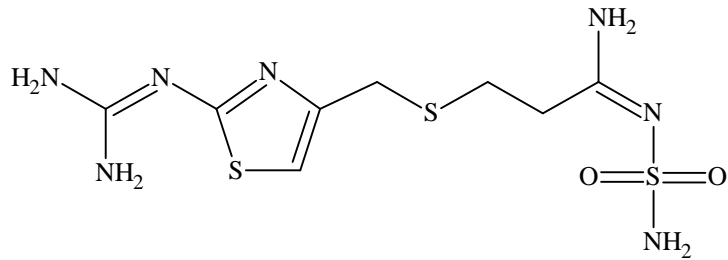
II. Gastrointestinal --\$1 billion/yr OTC

A. Antacids - neutralize stomach HCL - OTC

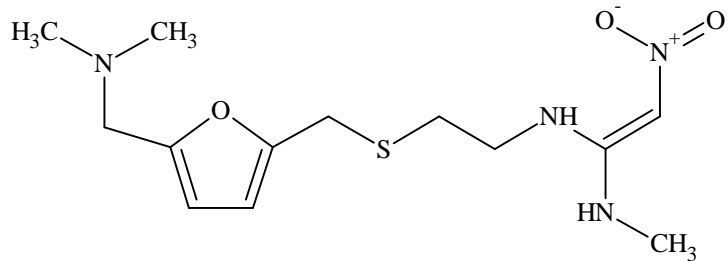
<u>Ingredient</u>	<u>Comments</u>
Al(OH) ₃	constipation
Mg(OH) ₂	laxative
CaCO ₃	constipation
NaHCO ₃	short relief time and acid rebound
AlMg(OH) ₅	
AlNaCO ₃ (OH) ₂	

B. Formerly prescription, now OTC

Cimetidine (Tagamet), Ranitidine (Zantac), and Famotidine (Pepcid) act to block action of histamine, which helps regulate gastric acid secretions



Famotidine



Ranitidine

C. Laxatives -- OTC

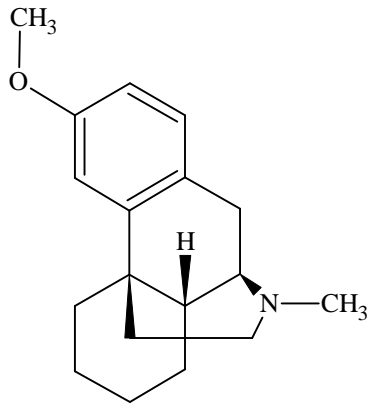
1. Bulk formers - absorb water and expand
pysillium seed preparations
2. Salines - bring water into the colon by osmotic action
magnesium hydroxide

3. wetting agents - draw water to the feces
dioteyl sodium sulfosuccinate
4. lubricants - soften the passage of the stool
mineral oil - causes depletion of fat soluble vitamins
5. stimulant or irritant - acts on the muscle itself
castor oil, phenolphthalein (removed from market),
bisacodyl

III. Cough and Cold >\$500 million/yr , with allergy and sinus over \$3 billion

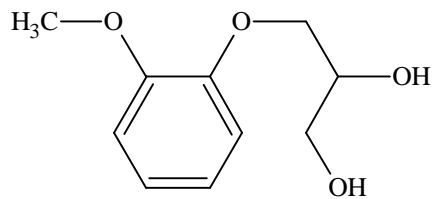
A. Cough

1. suppressant - dextromethorphan, codeine,
diphenhydramine



Dextromethorphan

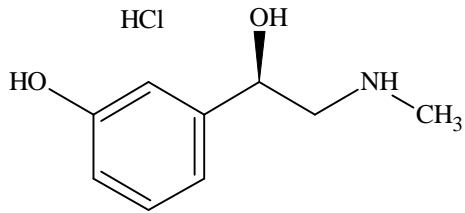
2. expectorant - guaifenesin



Guaifenesin

B. Congestion

1. pseudoephedrine
2. phenylpropanolamine (removed from market)
3. phenylephrine



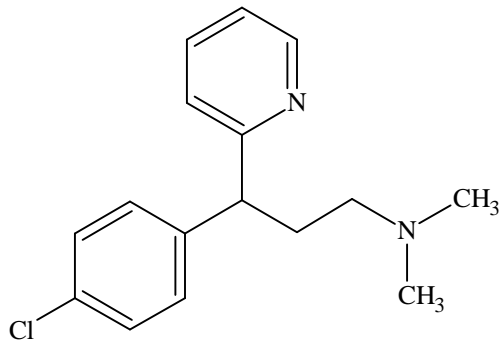
Phenylephrine Hydrochloride

C. Sneezing

1. antihistamines

chlorpheniramine maleate

doxylamine succinate



Chlorpheniramine

D. Pain relievers

1. acetaminophen

2. aspirin

3. ibuprofen

IV. Cardiovascular

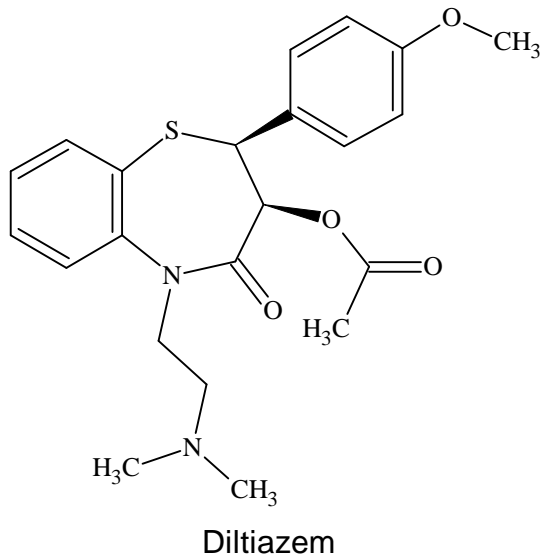
A. Conditions associated with heart disease

1. Atherosclerosis - buildup of plaque (cholesterol and fatty acids) on inner walls of arteries
2. Hypertension - heart must work harder, enlarges, needs more oxygen, angina results

B. Drugs

1. Diuretics - remove fluid by stimulating the production of urine (Dyazide)
2. Beta blockers - block action of epinephrine and norepinephrine at beta receptor sites. Heart is able to relax. This also decreases blood pressure.
[Propranolol (Inderal), metoprolol tartrate (Lopressor)]
3. Calcium channel blocking agents - Calcium ions in heart muscle trigger the contraction of the muscle. If these ions are blocked from entering the heart

muscle cells the heart relaxes and arteries dilate.
[Diltiazem (Cardizem)]

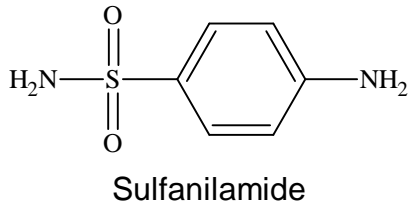


4. Vasodilators [nitroglycerin] Acts by releasing NO, a messenger molecule which dilates blood vessels.
Comment – research into the action of NO lead to the development of the anti-impotence drug Viagra.
5. Cholesterol lowering [niacin, and lovastatin]

V. Antibacterial drugs

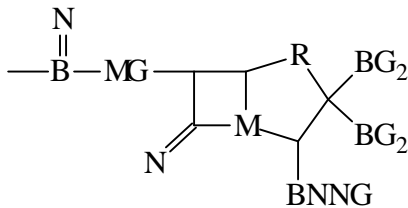
- A. sulfa - developed and used in WWII, now used predominantly for urinary tract infections

1. sulfanilamide

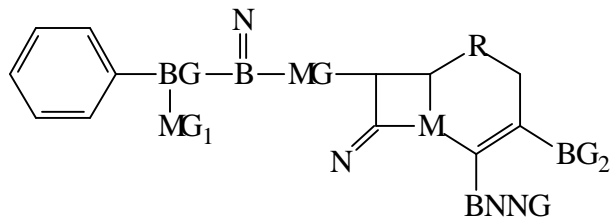


B. Penicillins - also called antibiotics because it is produced by a living organism and kills or inhibits the growth of other organisms

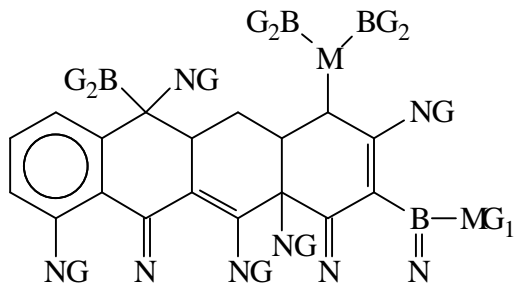
1. penicillin discovered in 1928 by Fleming



C. Cephalosporin - another antibiotic
Cephalexin (Keflex)



D. Tetracyclines - more broad based, have a fused ring system



Neurotransmitters – a class of compounds with little in common structurally but which are “messenger molecules” for nerve impulses.

Neurotransmitter:

Function

Acetylcholine

Bioactive amines:

Dopamine

fine muscle control, memory and emotion

Epinephrine (Adrenlin)

increases BP, dilates blood vessels

Norepinephrine

fine coordination of body movement and balance, mood, sleep cycle

Serotonin

mood, pain perception, sleep cycle

Histamine

Amino acids:

Glutamate

main “workhorse” of the brain

Glycine

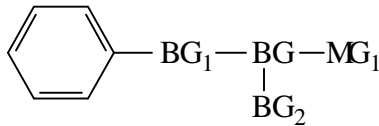
g-Aminobutiric acid (GABA)

another “workhorse” of the brain

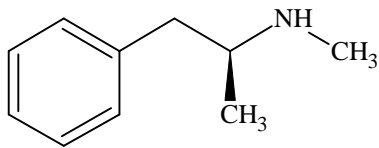
VI. Stimulants - increase activity and thought. Many elevate mood by elevation of norepinephrine, serotonin, and dopamine.

A. Amphetamines - similar to norepinephrine (a neurotransmitter)

Raise glucose level - depressing hunger



Amphetamine



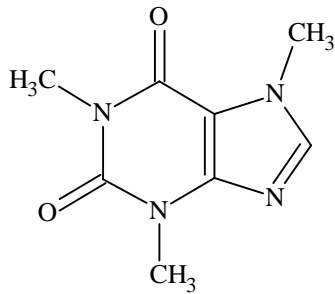
Methamphetamine

B. Caffeine

Increases heartbeat and metabolism, promotes secretion of stomach acid, increases production of urine – enhances action of glutamate neurotransmitter.

Mildly addicting - withdrawal symptoms include headache and depression

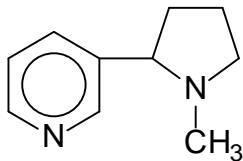
dosage - 110 mg in 5 oz coffee, 40 mg in 12 oz of cola drink, 6 mg in 1 oz of chocolate



Caffeine

C. Nicotine - tobacco

Average cigarette has 0.5 to 2.0 mg
addicting - prolonged withdrawal

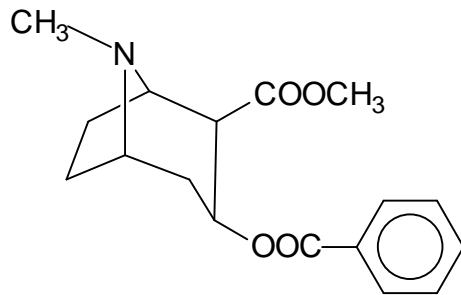


D. Cocaine

rapid absorption through mucous membranes
("snorted")

relaxes muscles of bronchial airways for easier breathing but nasty rebound

powerful stimulant for short time (1 hr), afterwards depression



VII. Depressants - decrease activity and thought, also called sedative-hypnotics – enhances the action of the neurotransmitter GABA.

A. Response with increasing dose

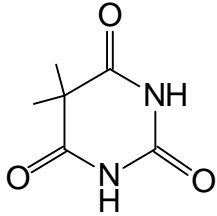
relief from anxiety --->disinhibition--->sedation

(relaxation) ---> sleep (hypnosis) --->anesthesia --->

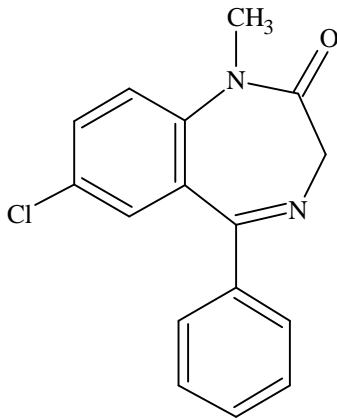
coma ---> death

B. Barbiturates

are addicting but dosage is higher than is needed for sedation



C. Benzodiazepines (Librium and Valium)



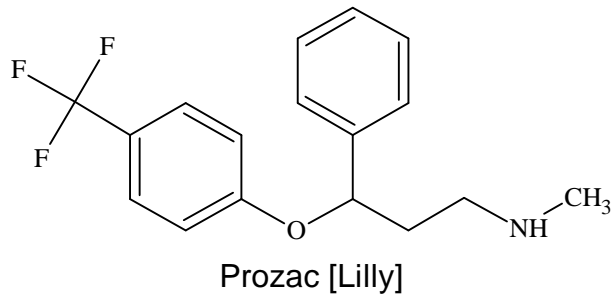
Valium [Roche]

Both groups of drugs act at the receptors for GABA, enhancing its effect (just like ethanol). GABA tends to reduce nerve transmission.

Antidepressants (>\$1 billion in sales)

Depression seems to involve a deficiency of norepinephrine and serotonin (and perhaps dopamine).

1. Amitriptyline prevents reuptake of both.
2. MAO (monoamine oxidase) inhibitors prevent conversion of neurotransmitter to inactive form.
3. Most popular is Prozac, which works by enhancing the effect of serotonin, blocking its reabsorption by cells.



VIII. Ethanol and Marijuana

A. Ethanol

depressant (acts to enhance GABA)

absorbed from the stomach

legal dose is 0.10% (m/v) in 46 states

addictive

Metabolism

ethanol to acetaldehyde (toxic) reaction is fast

acetaldehyde to acetic acid (slower)

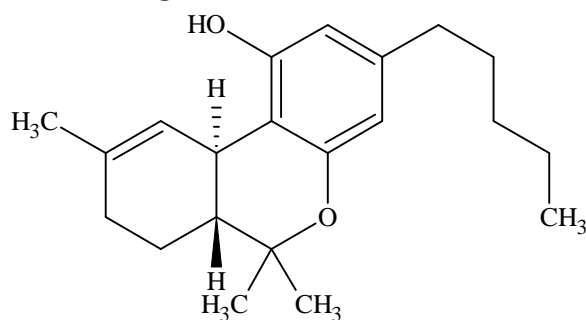
acetic acid to carbon dioxide and water in cells

B. Marijuana

depressant at low concentrations, hallucinogen at higher doses

major active ingredient is tetrahydrocannabinol

high doses lead to dependence



Tetrahydrocannabinol

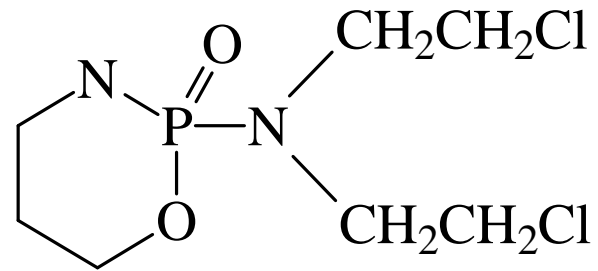
IX. Cancer Drugs

A. Treatment

1. Surgery
2. Radiation
3. Chemotherapy

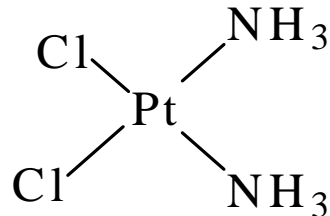
B. Chemotherapy

1. cyclophosphamide (alkylating agent)



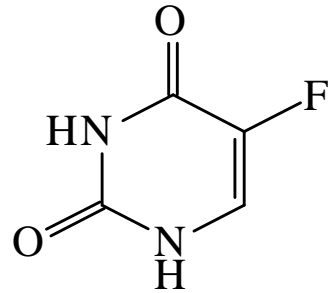
Action: transfers alkyl groups to Nitrogen base (especially guanine); prevents DNA replication. Kills both good and bad cells but effect is greater on cancer cells.

2. cisplatin



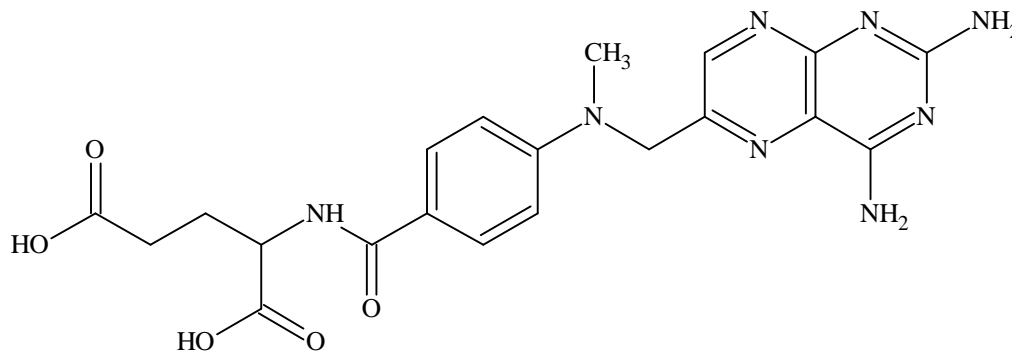
Action: Binds to N sites on guanine in DNA and prevents replication

3. 5-fluorouracil (antimetabolite) \Rightarrow breast cancer



Action: Involvement in nucleotide synthesis; inhibits formation of a thymine-containing nucleotide necessary for DNA synthesis.

4. methotrexate (antimetabolite) \Rightarrow leukemia

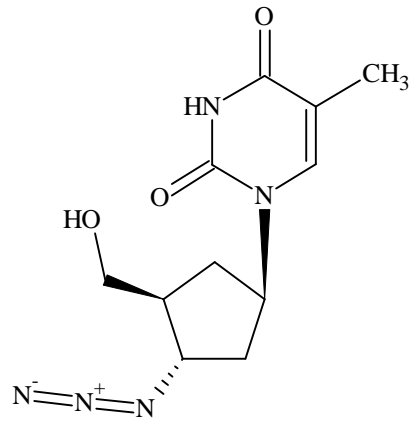


Methotrexate

Action: Blocks reduction of folic acid that is one of the first steps in nucleic acid synthesis.

AIDS (Acquired Immune Deficiency Syndrome)

- A. AIDS caused by HIV retrovirus, virus with an outer double layer of lipid material that acts as an envelope for proteins, the enzyme reverse transcriptase, and RNA
- B. Retrovirus penetrates T cell of immune system and reverse transcriptase changes DNA of T cell
- C. T cell produces more AIDS viruses and finally dies
- D. Drugs used against AIDS
 - 1. Nucleoside analogs. AZT (Azidothymidine) is accepted by reverse transcriptase in place of thymidine (nucleoside of thymine) and stops production



Azidothymidine

2. Reverse transcriptase inhibitors stop the reverse transcriptase
3. Protease inhibitors block the enzyme protease so that new copies of the virus can't infect new cells