Chemistry in Medicine

CHM 105 Applications Project

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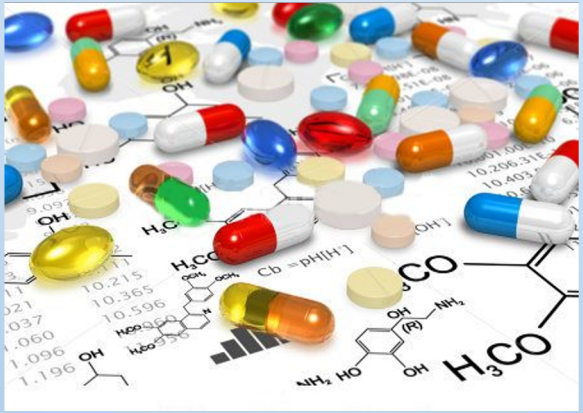
Table of Contents



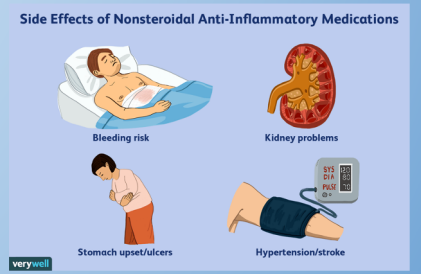
Introduction

Medicinal chemistry combines to form a set of highly interdisciplinary sciences, setting its physical, organic, and computational emphases alongside biological areas. Chemistry is necessary in order to study medicine and the drugs we use everyday to feel better and healthy. In this project, we look at the science of design and chemical synthesis focusing mainly on small organic molecules and their development of pharmaceutical drugs. A functional group is a portion of a molecule that is a recognizable group of bound atoms. For each drug, we list the functional groups found to show how each drug is categorized and unique in its own way. Many chemical compounds can be used and are used in pharmaceutical drugs. Organic chemistry gives people a strong basis for understanding acid-base imbalances within the body and how different medications work.

Drugs and Their Categories:

The first category of drugs is opioids. Opioids in medicine are prescription drugs used as pain relievers. These drugs bind to opioid receptors in the body. They make people feel relaxed and “high,” which is why there are some opioids that are illegal. Some opioids that this presentation includes are: Morphine, OxyContin, Codeine, and Demerol.

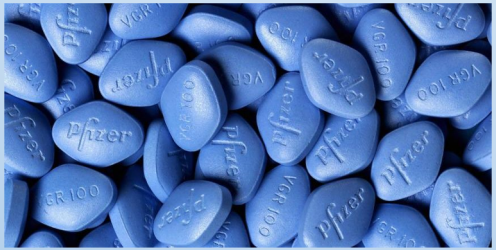
The second drug category of drugs is NSAIDs. These drugs are the most prescribed medications for treating conditions such as arthritis. They are more than just pain relievers. They are also non-opioid analgesics. Some NSAIDs in this presentation include: Aspirin and Rofecoxib.



Drugs and Their Categories:

The other medications are a part of different categories. Penicillin is an example of an antibiotic. These drugs fight bacteria within the body. Other examples of antibiotics include Cephalosporins and Tetracyclines.

Viagra is an example of phosphodiesterase inhibitors, which help treat erectile dysfunction in men. Other examples of phosphodiesterase inhibitors include Cialis and Levitra.



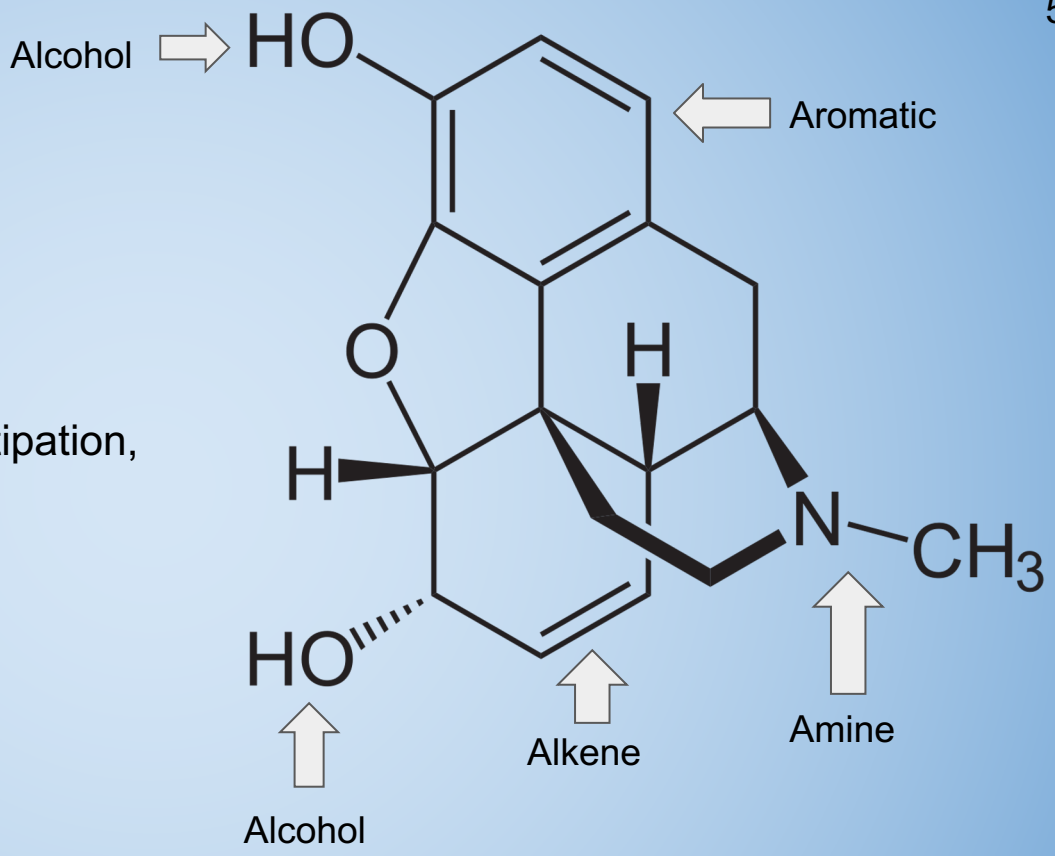
Cisplatin is an example of a chemotherapy drug (“antineoplastic”), and is classified as an “alkylating agent.” These drugs prevent cells from reproducing by damaging their DNA. Other examples of alkylating agents include Nitrosoureas, such as Carmustine, and Triazines, such as Dacarbazine.

Drugs and Their Categories:

Valium is an example of a Benzodiazepine. These drugs act as a sedative, so they slow down the body's functions. They do so by increasing the effect of GABA in the brain, which further inhibits signals and nervous system activities. Other examples of Benzodiazepine include Alprazolam (Xanax) and Clonazepam (Klonopin).

Norethindrone is an example of a progestin. These drugs stop the lining of the uterus from growing, which causes the uterus to produce certain hormones. They are a synthetic form of progesterone, which is a female hormone that regulates ovulation and menstruation. Other examples of progestins include Etonogestrel (Implanon) and Drospirenone (Slynd).

Morphine



Uses: Treat severe pain

Misuses: No common misuses

Side Effects: Nausea, vomiting, constipation, dizziness, increased sweating, lightheadedness

Functional Groups:

- Alcohol
- Alkene
- Amine
- Aromatic

Morphine

Discovered: Morphine was first discovered in Einback, Germany in 1805 by Freidrich Wilhelm Adam Serturner

First use: First used in a study in 1818 but it became widely available in the mid 1820's

Derived from: Morphine is a naturally occurring substance derived from the opium poppy plant

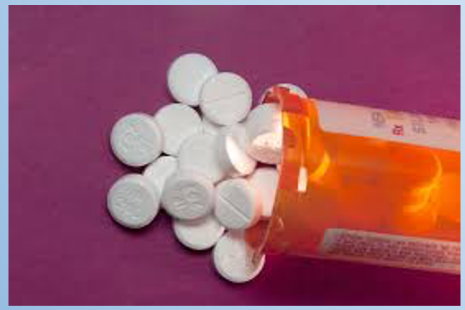
FDA approved: 1985

Locations used: Almost everywhere

Morphine

Mechanism

- Morphine works by binding to the opioid receptors mu, delta, and kappa
- The majority of the drugs effects are caused by the binding to the mu receptor, located in the Central Nervous System and Peripheral Nervous System
- Morphine inhibits descending inhibitory pathways of both the Central Nervous System and Peripheral Nervous System
- The body's pain transmissions are reduced
- The ability of morphine to numb pain is why it is sometimes abused



OxyContin

- *OxyContin is a specific brand name for the pain medication that contains the extended-release version of Oxycodone*

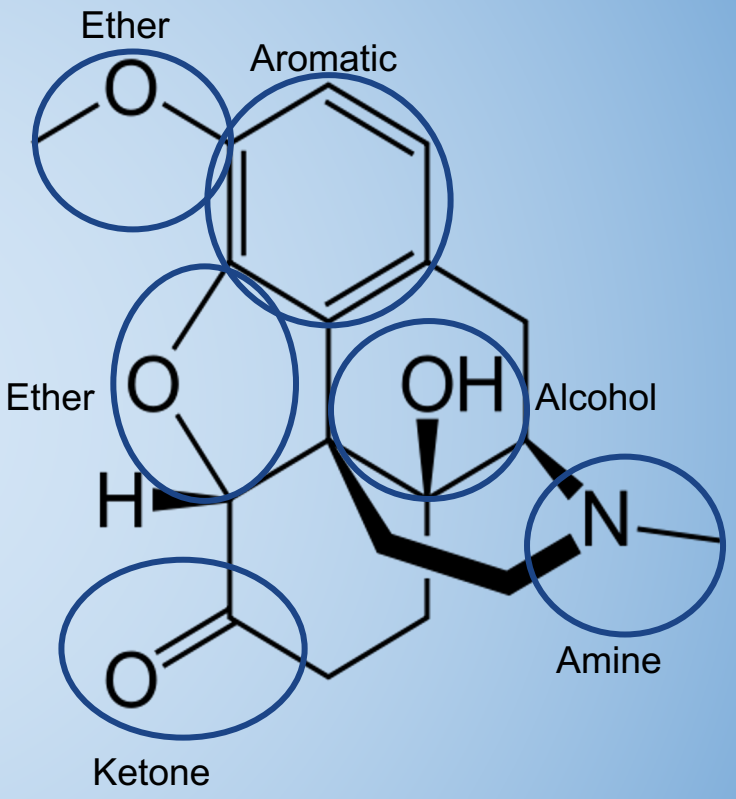
Uses: manage moderate to severe pain, long-acting medication; OxyContin is an opioid pain medication, or a narcotic

Misuses: overuse can lead to opioid addiction, respiratory depression, and potentially death

Side effects: nausea, dizziness, tiredness, headache, vomiting

Functional groups:

- Ether
- Aromatic
- Alcohol
- Ketone
- Amine



OxyContin

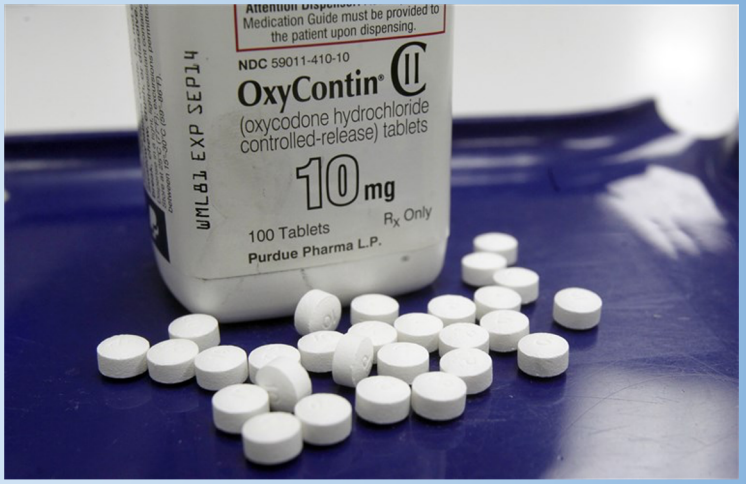
Discovered: OxyContin was first developed in Germany in 1916 from Thebaine (Paramorphine) as an alternative medication to heroin and morphine, which are addictive opioid drugs

First used: Came to United States in 1939, but became widely used in 1996 when Purdue Pharma began manufacturing it

Derived from: Thebaine, which is a natural opioid that is derived from the opium poppy plant; OxyContin is a semisynthetic opiate

FDA approved: December, 1995; still used today

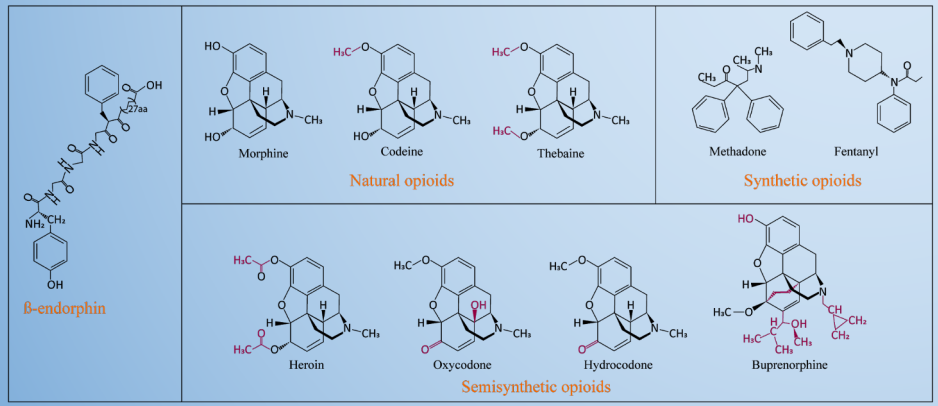
Locations used: Australia, Canada, Germany, Hong Kong, Japan, Singapore, United Kingdom, United States

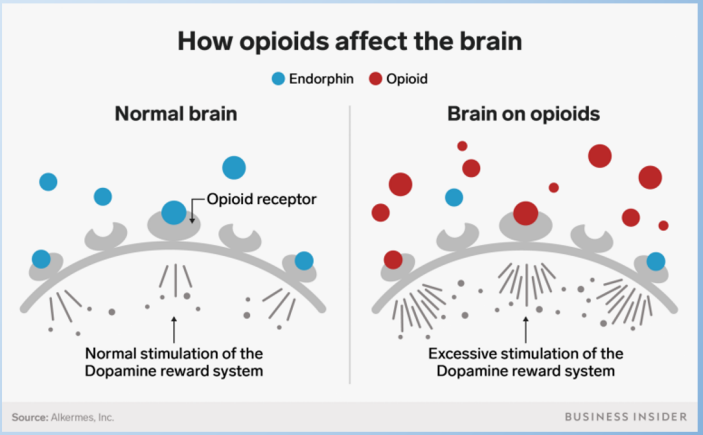


OxyContin

Mechanism:

- OxyContin works by binding to opioid receptors, which are found in the brain and spinal cord.
- It binds to G protein-coupled receptors (GPCRs), which trigger the brain to release endorphins.
- OxyContin resembles endorphins, which are natural substances in the brain that help relieve pain.
- Endorphins also stimulate the release of dopamine, which causes a feeling of euphoria.
- When OxyContin is used, it binds to opioid receptors on neurons that inhibit dopamine release, which results in a continuous release of dopamine.
- The release of dopamine is one reason opioid medications can potentially be addictive.





https://www.pursuecare.com/what-are-opioids-opioid-addiction/, Date accessed: April 17, 2020

Codeine

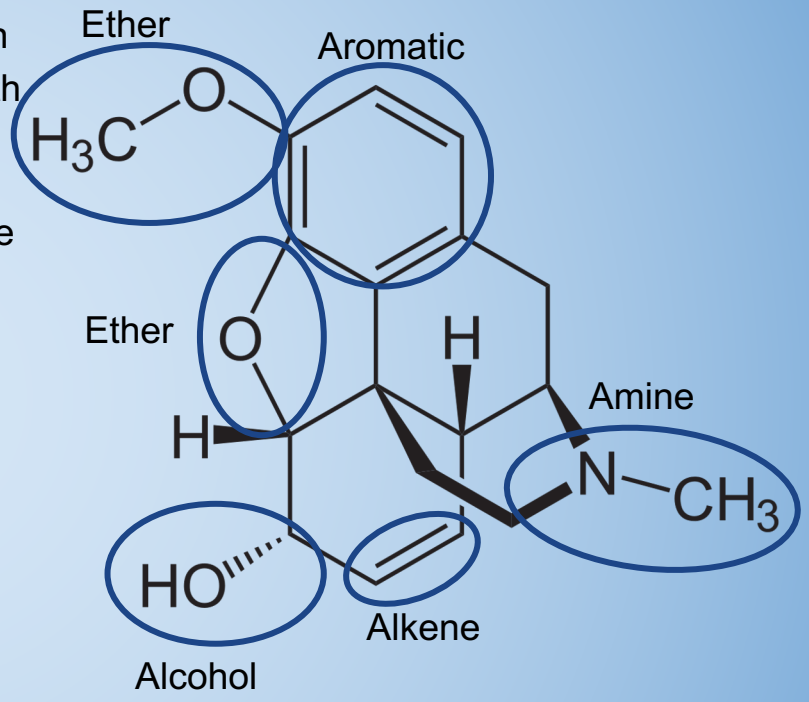
Uses: manage mild to moderate pain; Codeine is an opioid pain medication, or a narcotic; it can also be used in combination with other medication as a cough syrup to reduce coughing

Misuses: Codeine is not as potent as other opioids, but overuse can lead to an opioid addiction; long-term effects can lead to depression, anxiety, kidney damage, and potentially death

Side effects: headache, stomach pain, difficulty urinating, drowsiness, dizziness, nausea

Functional groups:

- Ether
- Aromatic
- Alcohol
- Alkene
- Amine



Codeine

Discovered: Codeine was first isolated in 1832 by French chemist Pierre Jean Robiquet.

First used: 1832

Derived from: Extracted directly from the opium poppy plant, but most of Codeine is extracted from Morphine, which is another opium derivative; Codeine is an opiate

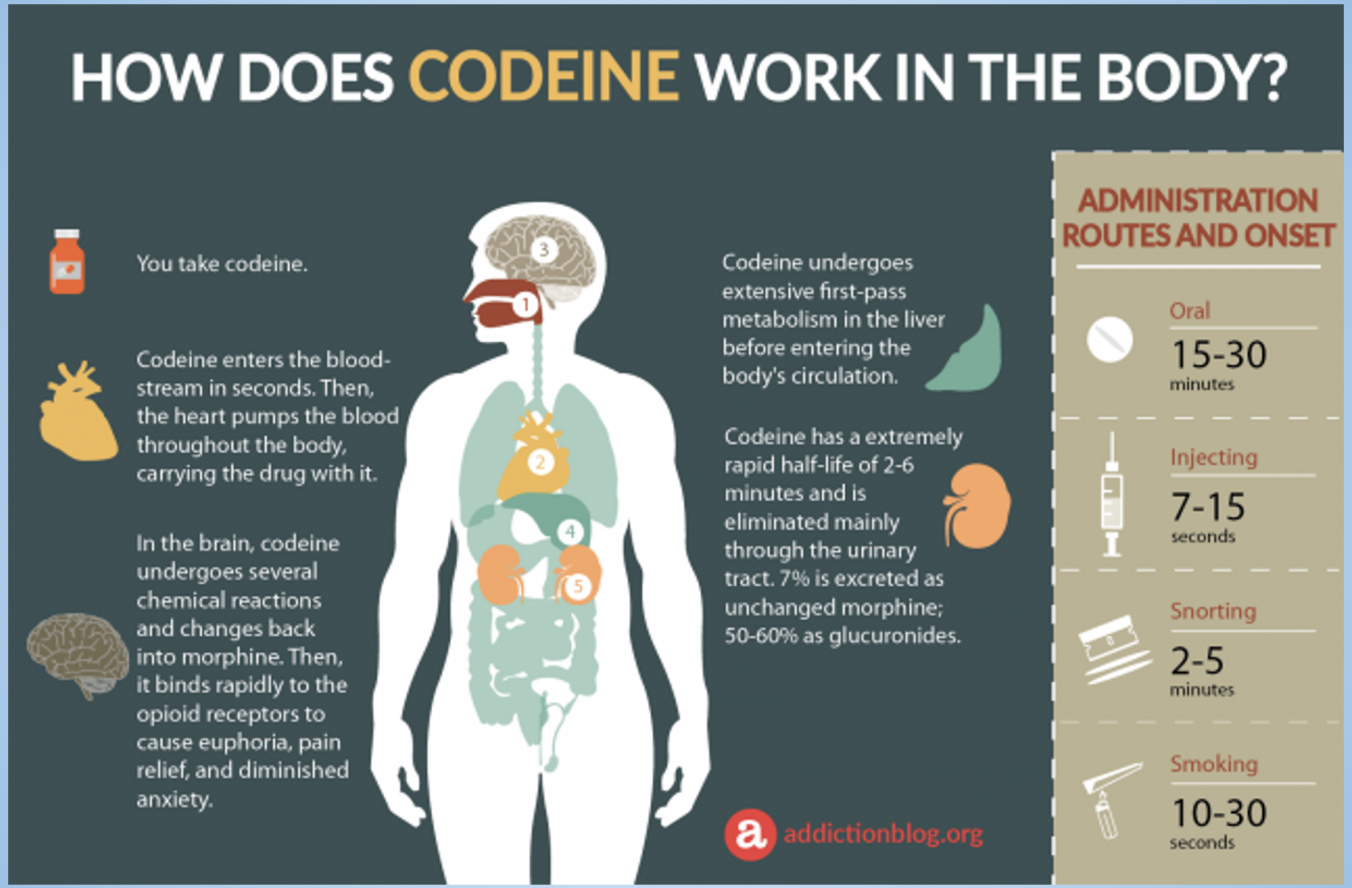
FDA approved: In 1848, Codeine was further inspected due to the Drug Importation Act. Since Codeine was widely used before there were more strict standards, there is no official FDA approval date. In 1971, the Controlled Substances Act further regulated Codeine and classified it as a Schedule II Controlled Substance. There have since been further modifications on Codeine's use.

Locations used: United Kingdom, France, South Africa, United States, Ireland

Codeine

Mechanism:

- Codeine works by binding to opioid receptors on pain signaling neurons.
- These opioid receptors are the G-protein coupled receptors. Once the drug binds to the site, endorphins are released, which relieves pain.
- Codeine resembles endorphins, which are naturally released to help relieve pain.
- Endorphins stimulate the release of dopamine, which causes a “feel-good” feeling.
- When Codeine is used, it binds to opioid receptors on neurons that inhibit dopamine release, which results in a continuous release of dopamine.
- Further, Codeine is useful to help reduce coughing by decreasing activity in the medulla oblongata, which is the part of the brain that causes coughing.
- Codeine is used as a cough suppressant and a sedative by acting on the medulla and decreasing its activity.



https://addictionblog.org/infographics/codeine-metabolism-how-does-codeine-work-in-the-body-infographic/, Date accesses: April 19, 2020

Demerol

Uses:

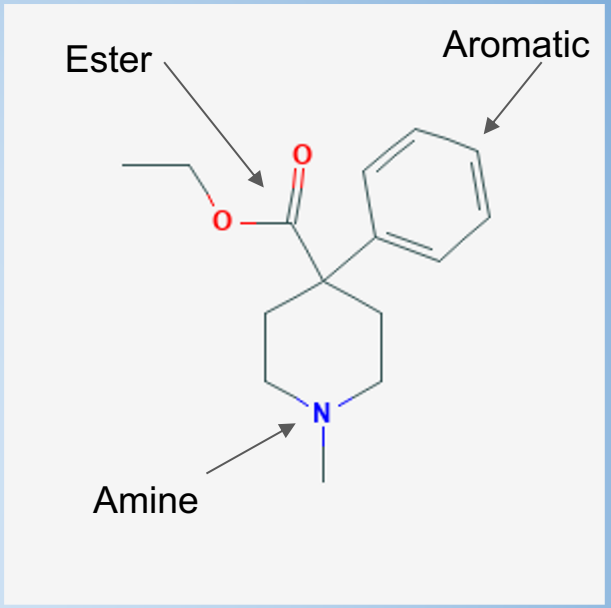
- Treat moderate to severe pain.
- Used before and during surgery or other procedures with other types of pain medication.
- Meperidine acts on certain centers in the brain to give you pain relief. This medication is a narcotic pain reliever similar to morphine.

Misuses:

- Used to treat long-term or ongoing pain
  - Should only be used to treat sudden episodes of moderate to severe pain

Mechanism:

- Demerol works by binding to the Opioid receptors in the brain and thereby blocking pain receptors from transmitting signals
- At the same time, Demerol releases feel-good neurotransmitters



Functional Groups:

- Aromatic
- Ester
- Amine

Demerol

Side Effects:

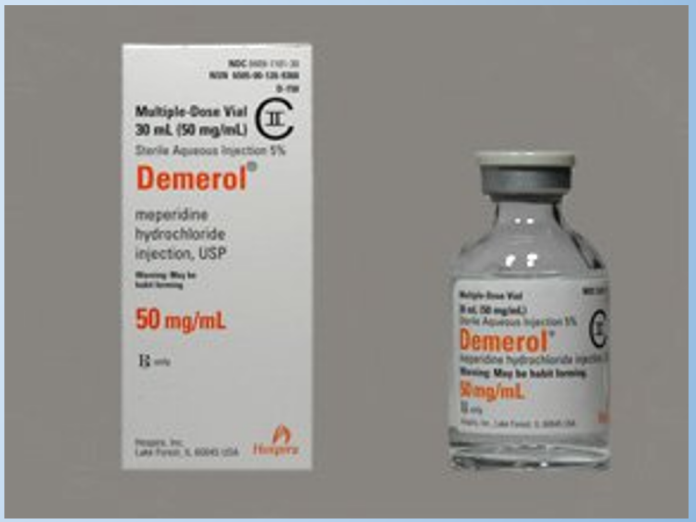
- Respiratory depression, circulatory depression, respiratory arrest, shock, and cardiac arrest
- Most frequently reactions: lightheadedness, dizziness, sedation, nausea, vomiting, and sweating

Discovered: 1932 for its anticholinergic effects and still used today

First Used: In an operation in 1942

Approved by FDA: 11/10/1942

Countries Used In: Almost all



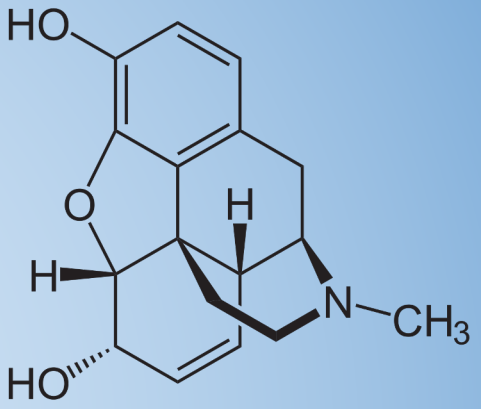
Demerol

Drug was Derived from:

- Meperidine, or pethidine, was originally synthesized from morphine in 1932 and considered a potential antispasmodic medication
- Meperidine was to be used to treat conditions such as asthma or allergies. Then, the pain-killing properties of meperidine led to a switch in focus, and it was viewed as a good alternative to morphine.

From a Drug:

- Morphine



Interesting Facts:

- Cannot be used during pregnancy
- One tenth as potent as morphine

Aspirin

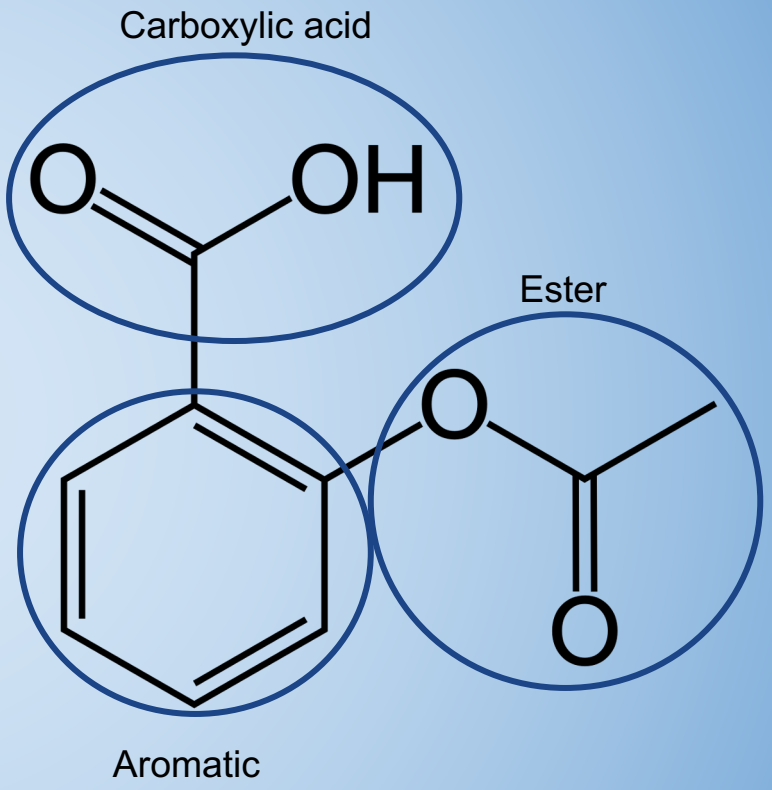
Uses: reduce a fever and inflammation, and relieve mild to moderate pain from conditions including headache, common cold, and muscle aches. Aspirin can also help reduce blood clots.

Misuses: overdose can lead to severe effects, including hives, bloody vomit, difficulty breathing, and swelling of lips, eyes, face, tongue, or throat

Side effects: vomiting, nausea, heartburn, stomach pain

Functional groups:

- Carboxylic acid
- Aromatic
- Ester

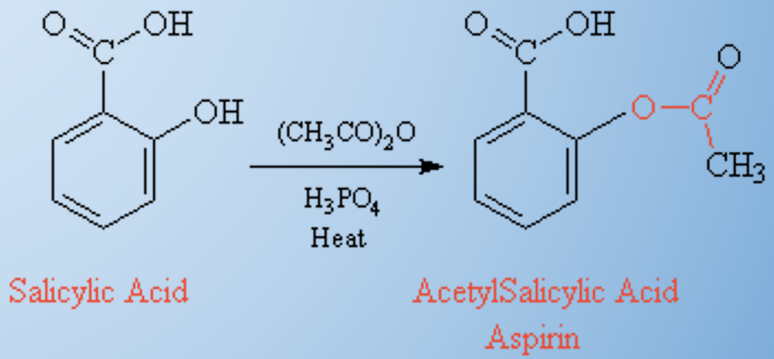


Aspirin

Discovered: In 1828, Joseph Buchner extracted the active ingredient from willow, which contains the natural compound that Aspirin is derived, and named it Salicin. In 1853, Charles Gerhardt chemically synthesized acetylsalicylic acid. In 1899, the pharmaceutical company Bayer named the drug Aspirin, for which it is known as today.

First used: In 1876, the first clinical trial was performed.

Derived from: Aspirin contains salicylate, which is derived from willow bark. Aspirin is prepared by the esterification of the phenolic hydroxyl group of salicylic acid.



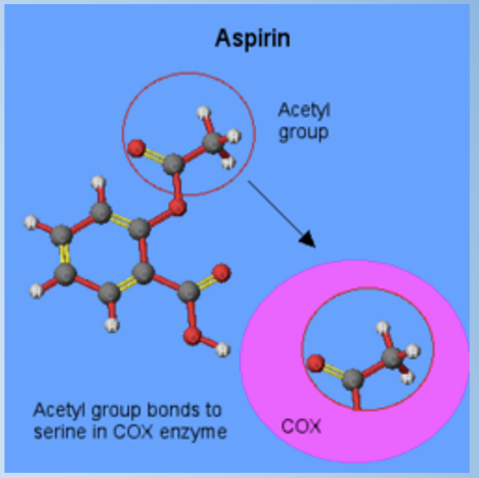
FDA approved: 1980

Locations used: Germany, United States, Europe, Latin America

Aspirin

Mechanism:

- Aspirin helps reduce pain and inflammation by blocking the production of prostaglandins, which are cells that regulate pain and inflammation.
- Further, the active ingredient in Aspirin, acetylsalicylic acid, inhibits fatty acid cyclooxygenase by acetylation of the active site of the enzyme. Aspirin interrupts the interaction between fatty acids and the enzyme cyclooxygenase (COX), which prevents the fatty acids from being transformed into pain messenger substances. Therefore, fewer pain messages are sent and the brain receives no pain signals, which reduces pain.
- When used to help decrease blood clots, Aspirin binds to COX-1 enzyme, which stops it from working. This interrupts the clotting process and helps prevent blood cells from clumping together.



Fun Facts:

- Medicines made from willow and other salicylate-rich plants have been used in ancient Sumer and ancient Egypt.
- Dogs are better able to tolerate Aspirin than cats are because cats lack the glucuronide conjugates that aid in the removal of Aspirin from the body, so cats metabolize Aspirin slowly.
- In 1950, Aspirin entered the Guinness World Records for being the most frequently sold painkiller.

Rofecoxib

Uses:

- It is in a class of drugs called nonsteroidal anti-inflammatory drugs (NSAID)
- It is used to reduce pain, inflammation, and stiffness caused by different forms of arthritis

Misuses: No common misuses

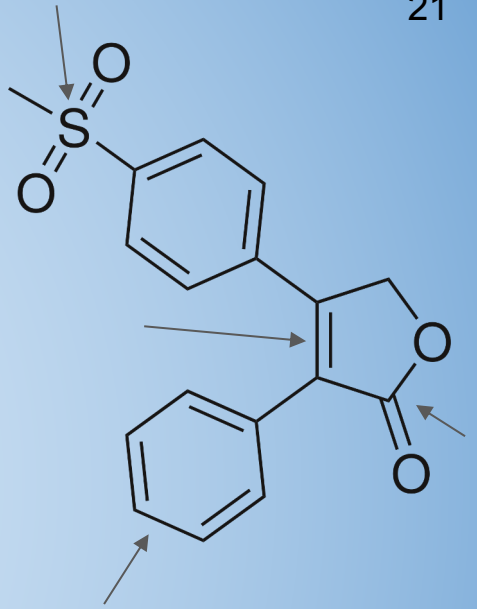
Discovered: 1992 by Merck and Searle

First Used: 1999

FDA Approval: May 20th,1999

Countries Used in: US, UK, several European countries

Side Effects: The most common side effects of rofecoxib are headache, abdominal pain, dyspepsia, diarrhea, nausea, heartburn and water retention.



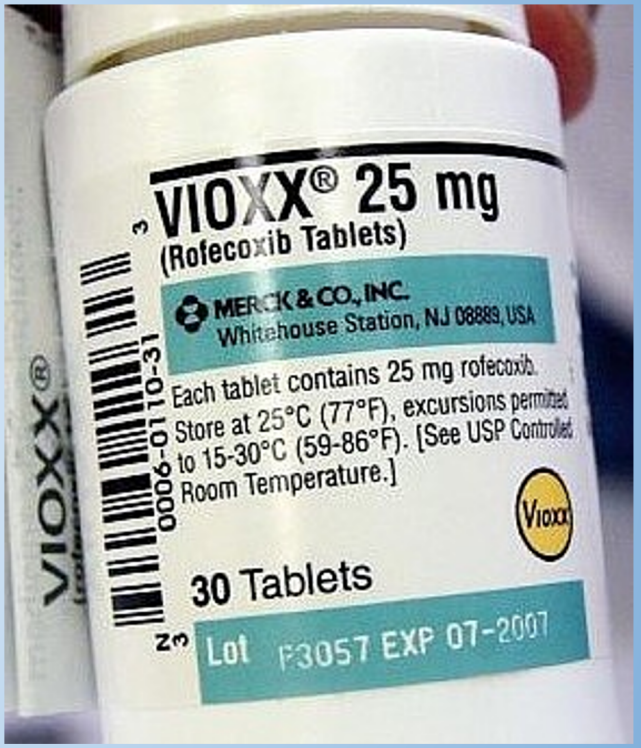
Functional Groups:

- Aromatic ring
- Ester
- Sulfone
- Alkene

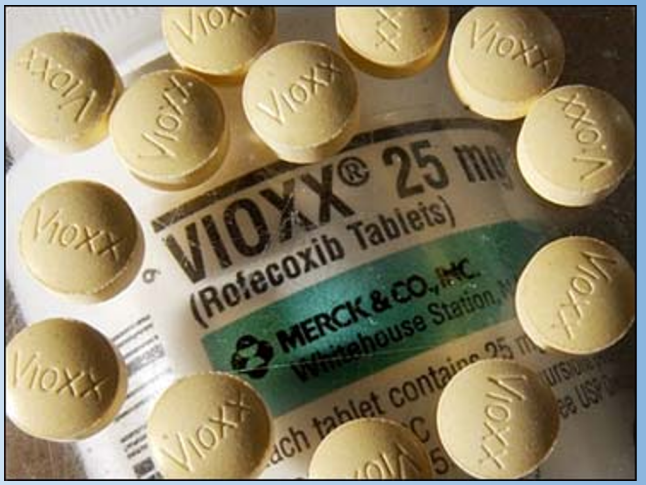
Rofecoxib

Mechanisms

- Rofecoxib lacks a sulfonamide chain and does not require CYP450 enzymes for metabolism.
- Like other NSAIDs, rofecoxib exhibits anti-inflammatory, analgesic, and antipyretic activity.
- NSAIDs appear to inhibit prostaglandin synthesis via the inhibition of cyclooxygenase (COX), which are responsible for catalyzing the formation of prostaglandins in the arachidonic acid pathway.
- Although the exact mechanisms have not been clearly established, NSAIDs exert their anti-inflammatory, analgesic, and antipyretic primarily through the inhibition of COX-2.

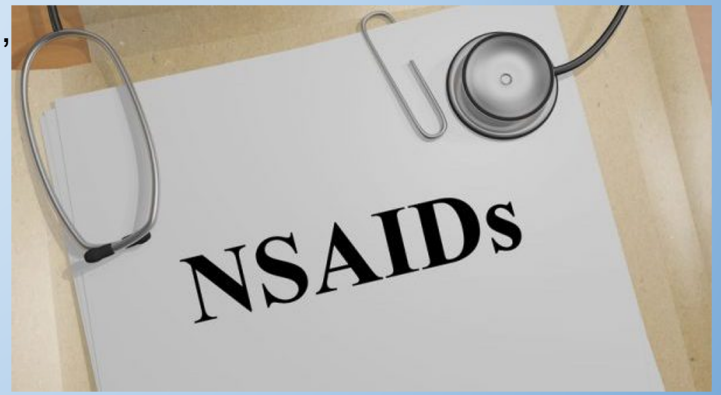


Rofecoxib



Drug was derived from

- Metabolites of the COX-2 inhibitor rofecoxib were prepared by synthetic or biosynthetic methods.
- Metabolites include products of oxidation, glucuronidation, reduction and hydrolytic ring opening.
- By creating "selective" NSAIDs that inhibit COX-2, but not COX-1, the same pain relief as traditional NSAIDs is offered, but with greatly reduced risk of fatal or debilitating peptic ulcers.
- Rofecoxib is a selective COX-2 inhibitor, or "coxib".

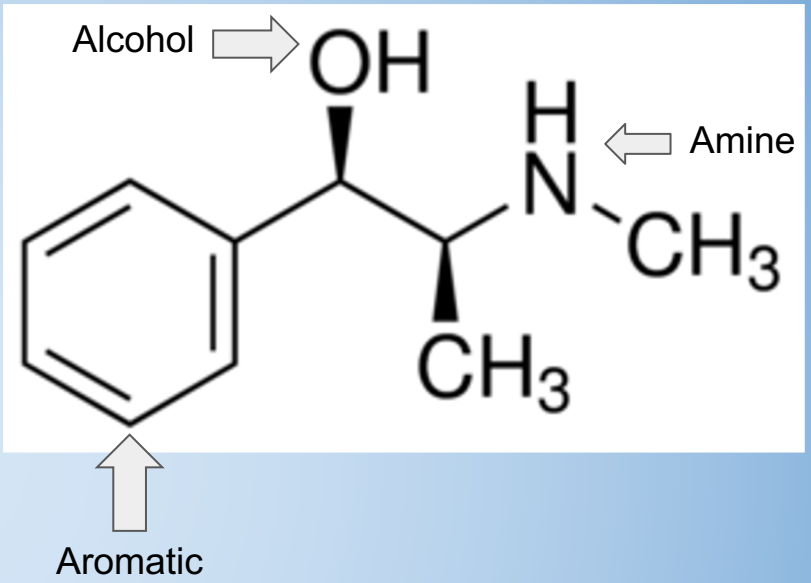


Ephedrine

Uses: temporary relief of short breath, chest tightness and wheezing as a result from bronchial asthma

Misuses: performance enhancement and weight loss

Side Effects: Blurred vision, dizziness, irregular heartbeat, headache, pounding in the ears or vomiting



Functional Groups:

- Aromatic
- Alcohol
- Amine

Ephedrine

Discovered: It was first isolated in 1885, it was forgotten about and rediscovered in the mid 1920s

First use: In 1930 it became a reliable asthma treatment

Derived from: It comes from the ephedra plant

FDA approved: The FDA banned products containing the drug in 2004. Ephedrine sulfate was approved in 2017

Locations used: Asia, United States

Ephedrine

Mechanism:

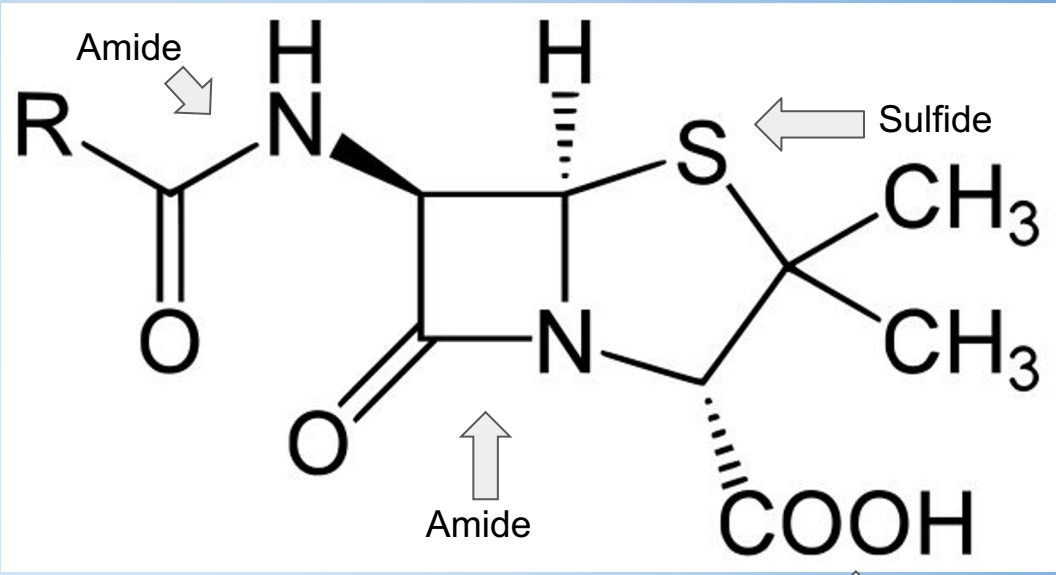
- Ephedrine binds to both alpha and beta receptors
- Stimulation of alpha-1-adrenergic receptors of smooth muscle within the vascular system ultimately results in a rise in vascular resistance which also rises both the systolic and diastolic blood pressure
- Stimulation of beta-1-receptors by ephedrine and norepinephrine increase cardiac chronotropy and inotropy
- Stimulation of beta-2-adrenergic receptors in the lungs results in bronchodilation

Penicillin

Uses: treat and prevent infections caused by bacteria

Misuses: There are no known misuses

Side Effects: upset stomach, nausea, vomiting, diarrhea, mouth sores



Functional Groups:

- Carboxylic Acid
- Sulfide
- Amide

Penicillin

Discovered: accidentally in 1928

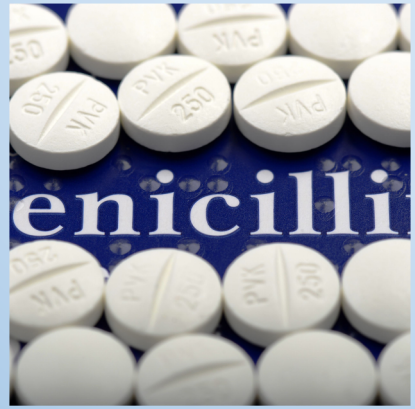
First use: First patient was treated on March 14,1942

Derived from: Penicillium mold

FDA approved: 03/02/1948

Locations used: Almost everywhere

Penicillin



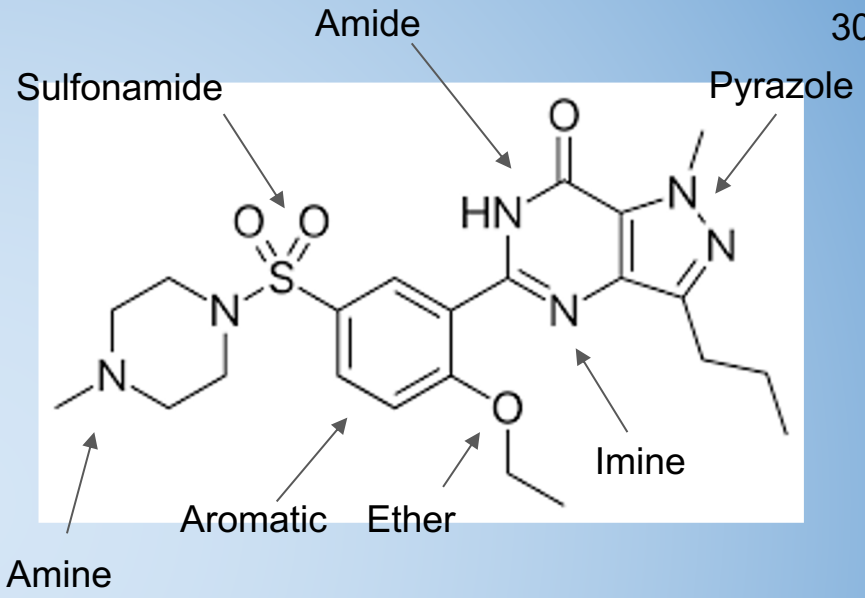
Mechanism:

- It inhibits bacterial cell wall synthesis by binding and inactivating proteins
- Penicillins inhibit the transpedidation reaction and it blocks the linking of the cell wall
- This results in the disintegration of the cell wall

Viagra

Mechanism:

- Increases blood flow to the penis so you can get and keep an erection hard enough for sex
- Works when you are sexually stimulated
- When someone has erectile dysfunction their nerves do not communicate with your brain properly and blood does not flow into the corpus cavernosa
- Relaxes the walls of your blood vessels and lets blood flow more easily to the parts of a penis that causes an erection.
- Sildenafil citrate attaches to the PDE5 enzyme in his penis and disables most of it
- When the man becomes sexually aroused, the brain sends the normal message to nerve cells in his penis, which produce nitric oxide as usual
- The nitric oxide creates cGMP, which starts relaxing the arteries in his penis



Functional Groups:

- Amide
- Ether
- Aromatic
- Amine
- Sulfonamide
- Pyrazole
- Imine

Viagra

Uses: Treat erectile dysfunction in men

Misuses: No common misuses

Discovered: 1996

First Used and Approved by FDA: March 27th, 1998 - Still used today

Countries Used in: Almost all (US, Canada, UK, etc.)

Interesting Facts: Works best on an empty stomach, helps with blood flow for Raynaud's, and is one of the most counterfeited drugs in the world

Side Effects: Headache, upset stomach, abnormal vision, back/muscle pain, nausea, loss of hearing and priapism

Viagra

Drug was derived from:

1. Sildenafil and was synthesized by a group of pharmaceutical chemists working at Pfizer's Sandwich, Kent, research facility in England.
2. It was initially studied for use in hypertension (high blood pressure) and angina pectoris (a symptom of ischemic heart disease).

From a plant:

Natural Viagra. It is native to the high Ande and it has always been used as a tonic plant by local populations. Its leaves are edible and can be chewed in high altitudes for a better physical performance.

Cisplatin

Uses:

- A chemotherapy medication used to treat a number of cancers
- Chemotherapy drug used to stop/slow cell growth

Misuses: No common misuses

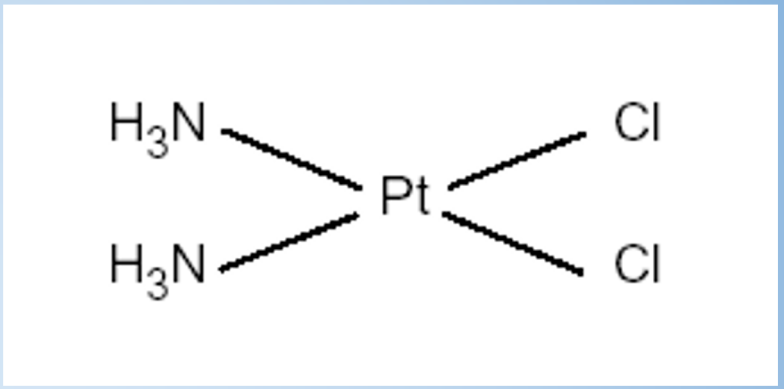
Discovered: 1845 by an Italian Chemist Michele Peyrone

First Used: 1978

FDA Approval: 12/19/1978

Countries Used in: US, UK, several European countries

Side Effects: Nausea, vomiting, hair loss, loss in taste, dark urine, decreased sweating, hearing loss, blood test abnormalities

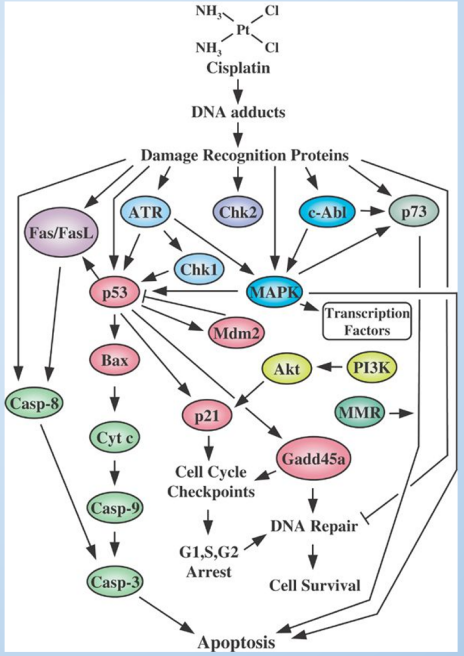


Functional Groups:
Pt2+ metal center with chloro and ammine ligands

Cisplatin

Mechanism:

- Cisplatin kills cancer cells by binding to DNA and interfering with its repair mechanism
- A molecule of water replaces one of the chloride ions. It then binds to a single nitrogen on a DNA nucleotide. The second chloride is replaced by another H_2O and the platinum binds to a second nucleotide
- Binding studies of cisplatin with DNA have indicated a preference for nitrogen 7 on two adjacent guanines on the same strand. It also binds to adenine and across strands to a lesser extent
- The cisplatin-DNA complex attracts the attention of high mobility group and other DNA repair proteins which become irreversibly bound
- The resulting distortion to the shape of the DNA prevents effective repair. (The trans isomer of cisplatin is unable to form 1,2 intrastrand links)
- Other antineoplastic agents contribute to the platinum-DNA-protein complex and synergistically reinforce the activity of cisplatin



https://www.nature.com/articles/1206933

Date accessed: 4/16/2020

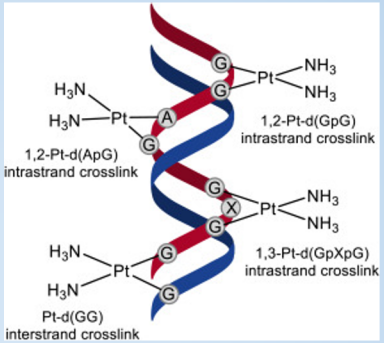
Cisplatin

Drug was Derived From:

- Cisplatin was accidentally discovered
- When doctors were testing platinum they realized that it stops bacterial cells from dividing
- Originally they thought they found a way to control cell growth with electricity
- However, it was the platinum blocking the compound from releasing the electrodes not the electricity
- Then, cisplatin was tested in mice to stop tumors and it worked, showing that with cisplatin the mice remained healthy and had no return of a tumor

From:

- Comes from platinum which is from a mineral cooperate



https://www.sciencedirect.com/topics/chemistry/cisplatin
Date accessed: 4/16/2020

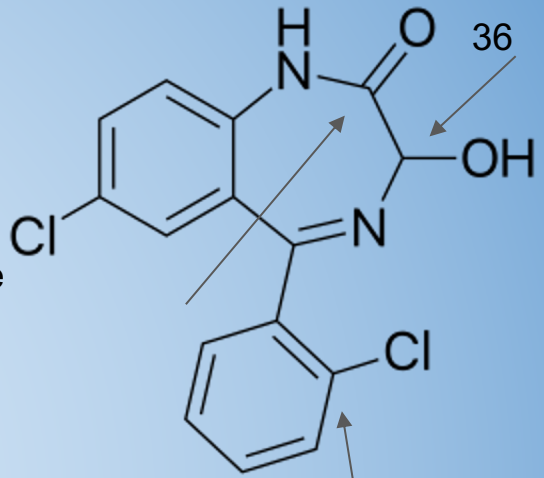
Interesting Facts:

- Its cure rate for cancer is more than 90%
- U.S. death rate from testicular cancer has dropped by two-thirds since 1975

Valium

Uses:

- Used to treat anxiety disorders, alcohol withdrawal symptoms, or muscle spasms.
- Can also be used to help treat seizures.



Functional groups:

- Amide
- Alcohol
- 2x chlorobenzene

Misuses: can cause addiction, overdose, or death

Discovered: 1959 by Hoffmann-La Roche

First Used: 1963

FDA Approval: 1960

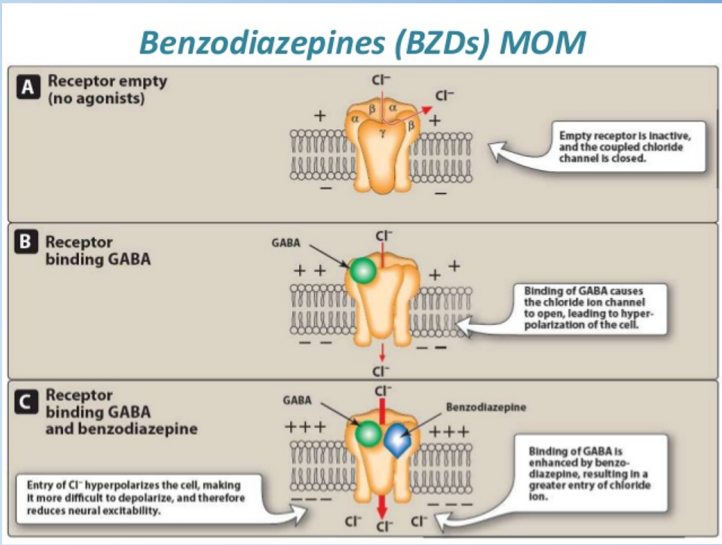
Countries Used in: US, UK, several European countries, Australia

Side Effects: weak or shallow breathing; severe drowsiness; depressed mood, thoughts of suicide; confusion, hallucinations; anxiety, panic attacks, trouble sleeping; hyperactivity, agitation, aggression

Valium

Mechanisms

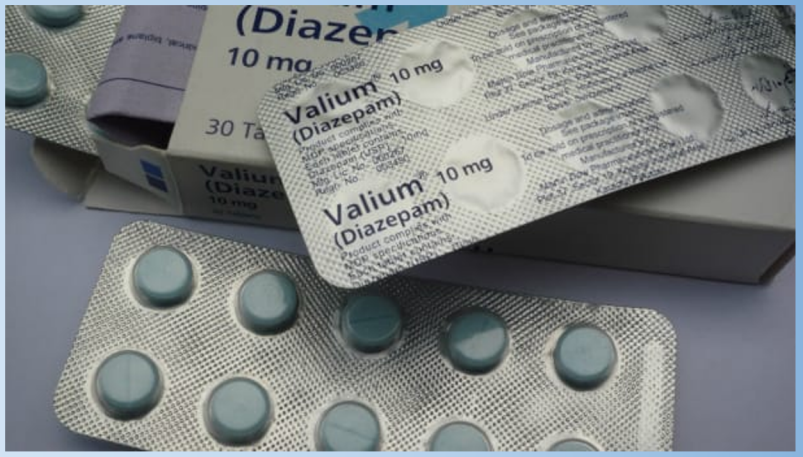
- Benzodiazepines are positive allosteric modulators of the GABA type A receptors
- The $GABA_A$ receptors are ligand-gated chloride-selective ion channels that are activated by GABA, the major inhibitory neurotransmitter in the brain.
- Binding of benzodiazepines to this receptor complex promotes binding of GABA, which in turn increases the total conduction of chloride ions across the neuronal cell membrane.
- This increased chloride ion influx hyperpolarizes the neuron's membrane potential.
- As a result, the difference between resting potential and threshold potential is increased and firing is less likely.
- This causes the arousal of the cortical and limbic systems in the CNS to be reduced

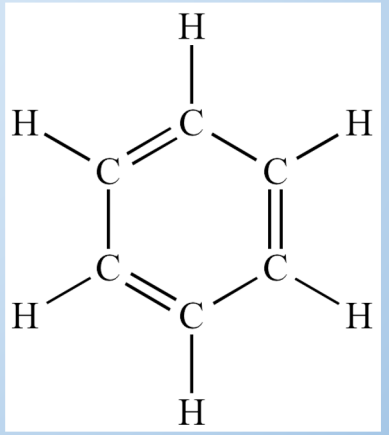


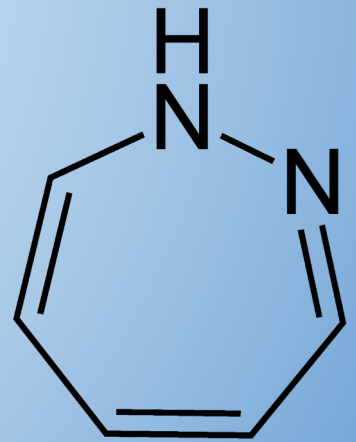
Valium

Drug was derived from:

- Its origins come from other sedatives and tranquilizers such as alcohol, bromides, chloral hydrates and more.
- Leo Sternbach was trusted with a task to find a new alternative that is less addictive.
- He created 40 new compounds that had no effect
- He modified one of the 40 compounds and forgot about it on a shelf for three years.
- After three years it was tested and showed similar results as the other sedatives.
- Valium is chemically derived from a benzene ring and a diazepine ring.







Norethindrone

Uses:

- Is a form of progesterone, a female hormone important in regulating ovulation.
- It is used for birth control

Misuses: No common misuses

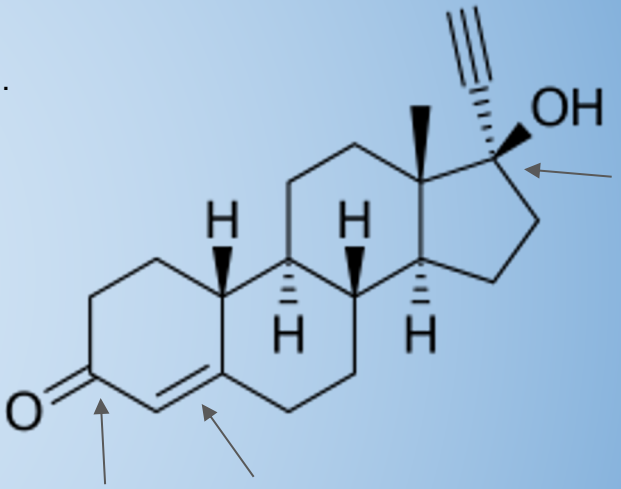
Discovered: 1951

First Used: 1957

FDA Approval: 1973

Countries Used in: Almost all

Side Effects: irregular vaginal bleeding, headache, stomach pain, depressed mood, weight gain.



Functional groups:

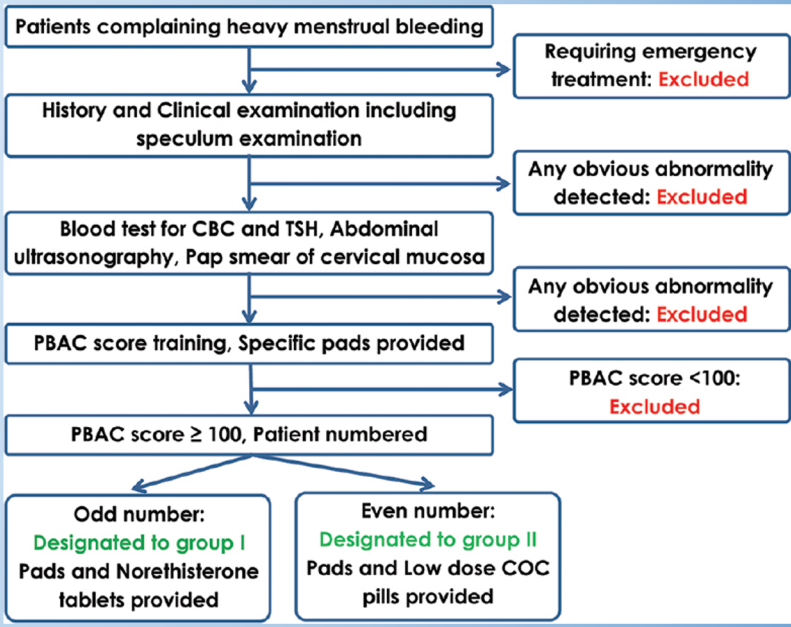
- **Alcohol**
- **Alkene**
- **Ketone**

Norethindrone

Mechanisms:

- Progestins enter the target cells through passive diffusion and bind to cytosolic receptors that are bound to the nucleus.
- The steroid receptor will initiate transcription, causing an increase in protein synthesis.
- Progestins will affect the serum concentrations of other hormones like estrogen.
- It can reduce the availability or stability of the hormone receptor complex or by turning off specific hormone-responsive genes by direct interaction with the progestin receptor in the nucleus.
- This will cause a negative feedback mechanism that inhibits estrogen receptors.

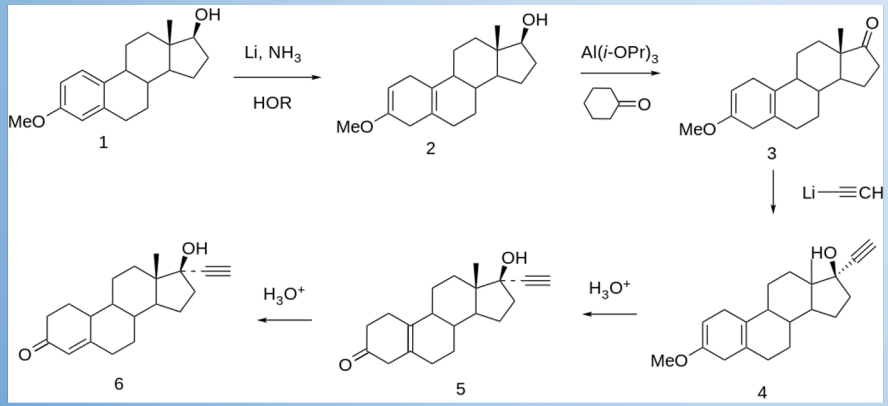
- The decrease in progesterone levels towards the end of the menstrual cycle contributes to the disintegration of the endometrium and much of this lining of the uterus, are expelled with vaginal bleeding .

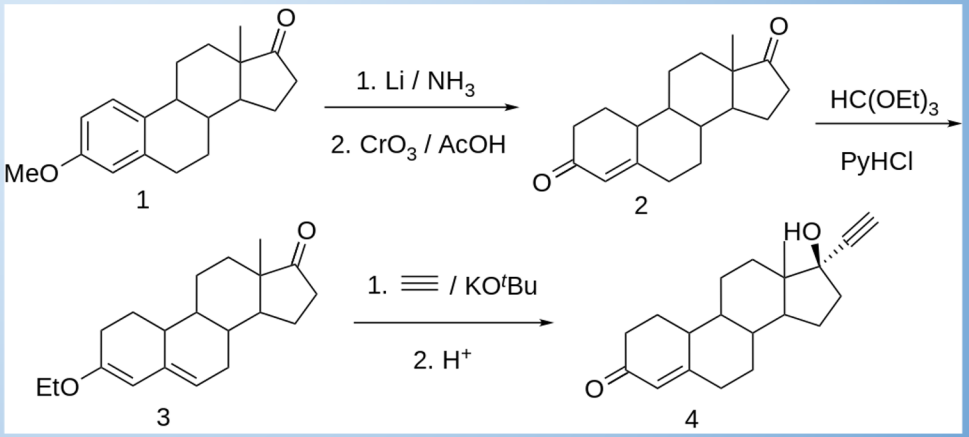


Norethindrone

Derived from:

- Norethisterone is a synthesized chemical.
- It is derived from ethisterone and has 20-fold greater potency as a progestogen.
- It is synthesized starting at Estradiol 3-methyl ether and ends with norethynodrel
- The other synthesis starts with estr-4-ene-3,17-dione and ends with the norethisterone.





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