

Chemicals in medicines

The words 'medicine' and 'drug' are often used in our country to mean the same substances: any substance, manufactured artificially, which can help recovery from sickness, relieve symptoms or modify a natural process in the body. A medicine is often a mixture of several chemical compounds. Even if it has only one active component compound often other substances are used as fillers or binders to give it bulk. Chemistry, the science related to chemical substances, provides us the tools to make and study the substances that are the constituents of almost all medicines. The past hundred years or so, ever since the advent of organic chemistry, many chemical compounds have been discovered in nature that are effective for curing diseases. Modern chemistry has also made it possible to synthesize several medicines using methods of organic chemistry.

The most common medicines can be classified into few groups, e.g. antibiotics; antiseptics; analgesics; and antipyretics etc. While an **antibiotic** is a drug that kills or prevents the growth of bacteria, an analgesic is often used to relieve pain.

There are very many medicines that come under each of these groups. Often several chemical compounds that make a particular group of medicines, say antibiotics have similar chemical structure. Since the medicines in a particular group are effective for treating a particular type of ailment or disease, their mode of action can also be very similar. But, the methods used to isolate a medicine from its natural sources or to synthesize it are most often very different.

In this project, I have tried to find out the relationships between chemical structures of medicines in three groups of medicines, viz. Antibiotics; Antipyretics and Analgesics. I have also explored the mode of action of these groups of medicines and the chemical methods used to make them available.

Antibiotics

Our body and our domestic animals, can serve as hosts to a wide variety of disease-causing organisms (**pathogens**): These are:

- bacteria

- viruses
- fungi
- protozoons

Here we will examine only those chemicals that are used to combat bacterial pathogens. An antibiotic (Greek anti, "against"; bios, "life"), is a chemical substance produced by one organism that is destructive to another. This process traditionally has been called antibiosis and is the opposite of symbiosis. More specifically, an antibiotic is a type of chemotherapeutic agent that has a toxic effect on certain types of disease-producing microorganisms without acting dangerously on the patient. The definition most used for antibiotics is: any substance produced by a microorganism which harms or kills another microorganism. However, antibiotics DO NOT harm viruses. Doctors often prescribe antibiotics when you may have a viral infection because of the possibility that you may also acquire a bacterial infection because you are so ill with a virus - being ill places a person at risk for certain bacterial infections that are normally handled without any problem.

The overwhelming majority of antibiotic substances are natural products that certain bacteria and fungi (molds) produce and send outside of their cells. About 90% of the antibiotics in use today, are isolated from bacteria. There are a few antibiotics, however, which are completely synthetic... that is, are made from scratch in the laboratory. These particular antibiotics are designed to inhibit some process previously identified to be completely unique to bacteria, and necessary for the bacterium to remain alive. An antibiotic can be most often classified into any one of the following categories of chemical compound:

1. Aminoglycosides
2. Glycopeptides
3. Beta Lactams also known as Penicillins
4. Tetracycline
5. Quinolones
6. Sulfonamides

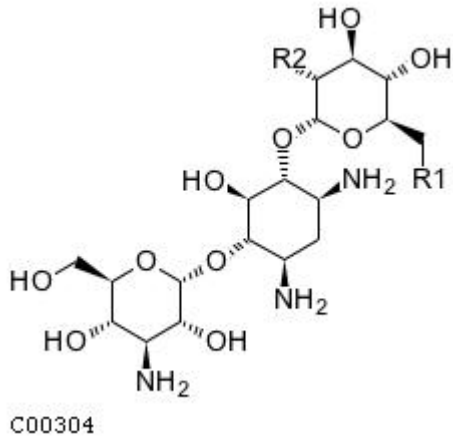
Aminoglycosides

Aminoglycosides are antibiotics that are often administered into veins or muscle to treat serious bacterial infections. Some aminoglycosides are also used orally to treat intestinal infections or topically to treat eye infections. Some very popular examples of this group of antibiotics are:

Examples are:

- Streptomycin
- Kanamycin
- Neomycin
- Gentamycin

The chemical structure of this group of antibiotics is:

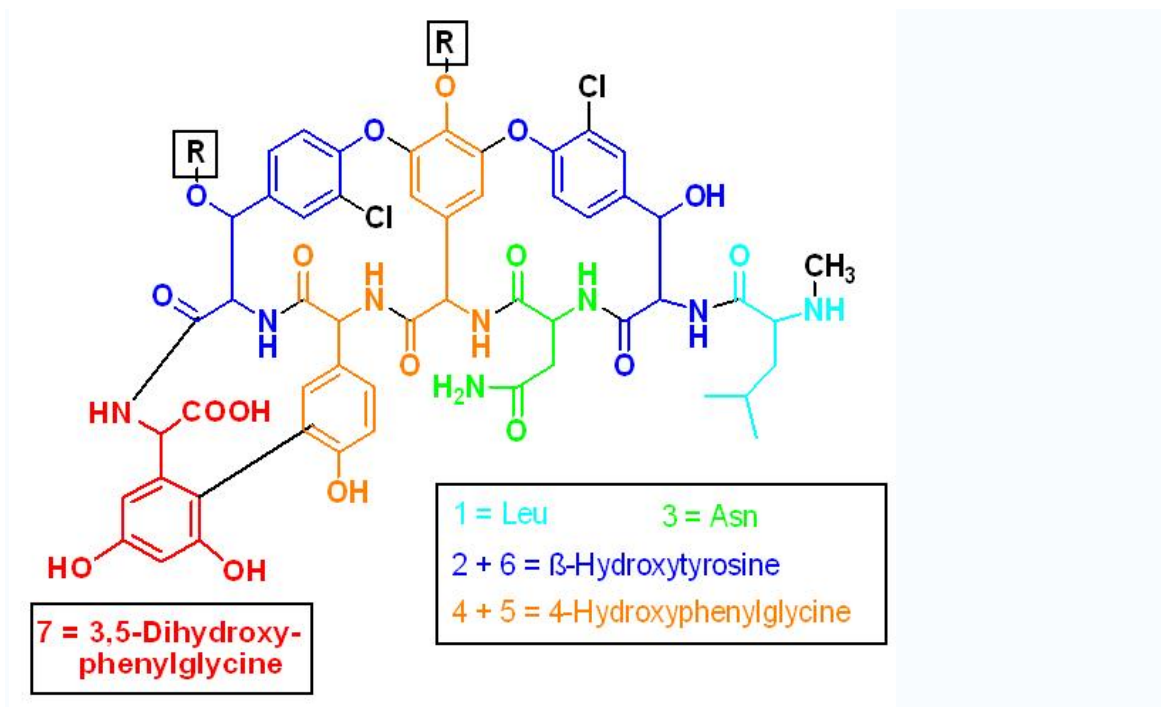


Glycopeptides

Glycopeptide antibiotics are a class of antibiotic drugs. They consist of a glycosylated cyclic or polycyclic [nonribosomal peptide](#). Important glycopeptide antibiotics include [vancomycin](#), [teicoplanin](#), [ramoplanin](#), and decaplanin.

This class of drugs inhibit the synthesis of cell walls in susceptible microbes by inhibiting peptidoglycan synthesis. Due to their toxicity, their use is restricted to those patients who are critically ill or who have a demonstrated hypersensitivity to the β -lactams.

The chemical structure of a glycopeptide antibiotic is



Penicillins are one major class of antibiotics. They are used to treat strep throat and countless other infections. Examples of various kinds of penicillins include

[Amoxicillin](#)

[Ampicillin](#)

[Azlocillin](#)

[Carbenicillin](#)

[Cloxacillin](#)

[Dicloxacillin](#)

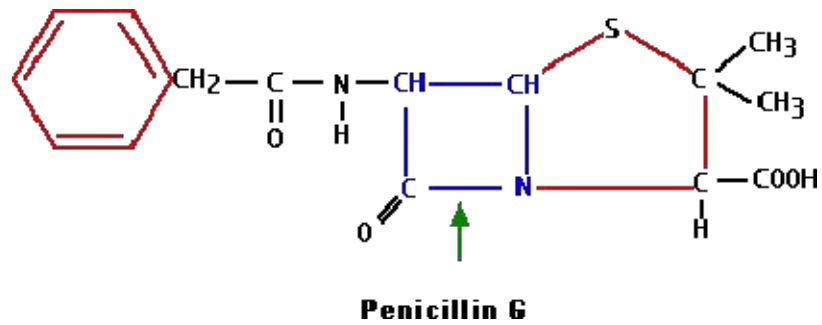
[Flucloxacillin](#)

[Mezlocillin](#)

[Nafcillin](#)

[Penicillin](#)

Common structural features of Beta-Lactams; (The beta-lactams get their name from the characteristic ring structure — shown here in blue — that they all share. (The green arrow shows the bond that is broken by a class of enzymes called beta-lactamases that are synthesized by many penicillin-resistant bacteria.)

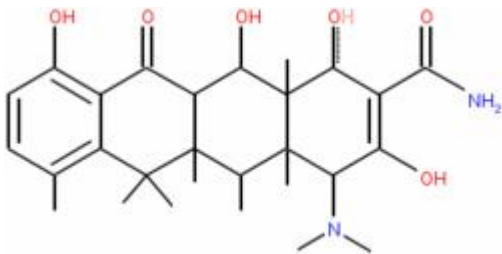


Tetracycline

Tetracyclines are another category of antibiotics. In addition to being used to treat infections, they are often used to manage acne. A few of the tetracyclines frequently used are:

- Achromycin V® (Tetracycline)
- Minocin® (Minocycline)
- Vibramycin® (Doxycycline)

The chemical structure of most tetracycline is related to the following structure. One can see that the name is derived from the fact that it is made up of four rings (cycles)



Examples of commonly used tetracycline's include:

[Demeclocycline](#)

[Doxycycline](#)

[Minocycline](#)

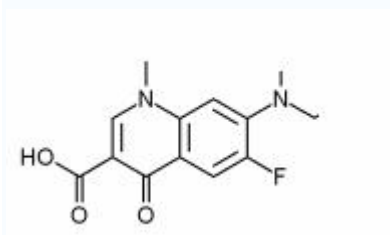
[Oxytetracycline](#)

[Tetracycline](#)

Quinolones

The **quinolones** are a family of broad-spectrum antibiotics. The parent of the group is nalidixic acid. The majority of quinolones in clinical use belong to the subset of **fluoroquinolones**, which have a fluoro group attached the central ring system. Quinolones and fluoroquinolones are bactericidal drugs, actively killing bacteria. Quinolones inhibit the bacterial DNA gyrase or the topoisomerase II enzyme, thereby inhibiting DNA replication and transcription.

The common chemical structure is as follows



Sulfonamides

Sulfonamide drugs (known widely as "sulfa drugs") were the first antibacterial antibiotics, and paved the way for the antibiotic revolution in medicine. The first sulfonamide was trade named Prontosil, which is a prodrug. Experiments with Prontosil began in 1932 in the laboratories of the Bayer Corporation, a component of the huge German chemical trust IG Farben. The dye-based drug was synthesized by Bayer chemist Josef Klarer and tested in animals under the direction of physician/researcher Gerhard Domagk. Domagk quickly won the 1939 Nobel Prize in Medicine and Physiology, an honor that Hitler forbade him to accept.

Some examples of sulfonamide antibiotics are:

[Mafenide](#)

[Prontosil](#)

[Sulfacetamide](#)

[Sulfamethizole](#)

[Sulfanilimide](#)

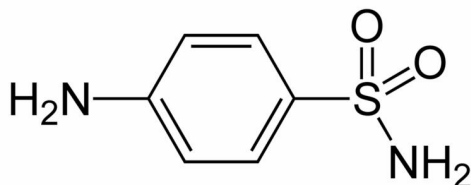
[Sulfasalazine](#)

[Sulfisoxazole](#)

[Trimethoprim](#)

[Trimethoprim-Sulfamethoxazole \(Co-trimoxazole\) \(TMP-SMX\)](#)

There common chemical structure is:

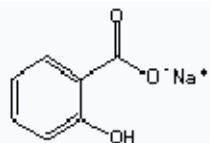


Analgesics

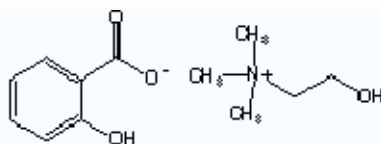
Analgesics are medicines that help to control pain and reduce fever. An **analgesic** (colloquially known as a **painkiller**) is any member of the diverse group of drugs used to relieve pain (achieve *analgesia*). This derives from Greek *an-*, "without", and *-algia*, "pain". Examples of analgesics that are available over the counter are: aspirin, acetaminophen, ibuprofen, ketoprofen and naproxen sodium. Some analgesics contain a combination of ingredients in one pill, such as aspirin, acetaminophen and caffeine.

Analgesics act in various ways on the peripheral and central nervous system; they include paracetamol (acetaminophen), the [nonsteroidal anti-inflammatory drugs](#) (NSAIDs) such as the salicylates, narcotic drugs such as [morphine](#), synthetic drugs with narcotic properties such as tramadol, and various others. Some other classes of drugs not normally considered analgesics are used to treat [neuropathic](#) pain syndromes; these include tricyclic antidepressants and anticonvulsants.

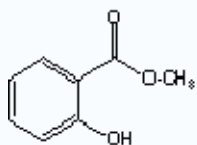
Thus acetylsalicylic acid (commonly known as aspirin) is a salicylate with the chemical structure:



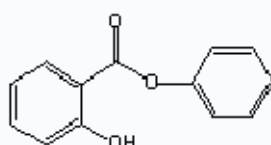
sodium salicylate



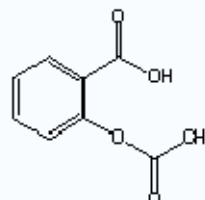
choline salicylate (Tilisate[®])



methylsalicylate
(Oil of Wintergreen)

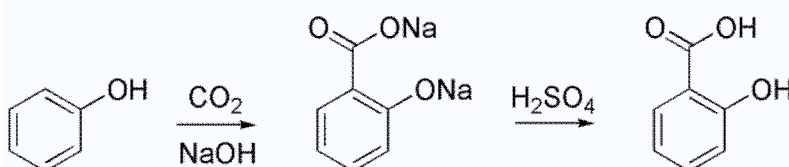


phenyl salicylate
(a "sabl")



acetylsalicylic acid
(aspirin)

Aspirin is commercially synthesized using a two-step process. First, phenol (generally extracted from coal tar) is treated with a sodium base generating sodium phenoxide, which is then reacted with carbon dioxide under high temperature and pressure to yield salicylate, which is acidified, yielding salicylic acid. This process is known as the Kolbe-Schmitt reaction.



Antiseptics

Antiseptics are antimicrobial substances that are applied to living [tissue/skin](#) to reduce the possibility of infection, sepsis, or putrefaction. They should generally be distinguished from *antibiotics* that destroy microorganisms within the body, and from *disinfectants*, which destroy microorganisms found on non-living objects. Some antiseptics are true *germicides*, capable of destroying microbes ([bacteriocidal](#)), whilst others are [bacteriostatic](#) and only prevent or inhibit their growth. *Antibacterials* are antiseptics that only act against bacteria.

Some chemical compounds/groups of chemical substances that are often used as antiseptics are:

- [Alcohols](#)

Most commonly used are ethanol (60-90%), 1-propanol (60-70%) and 2-propanol/isopropanol (70-80%) or mixtures of these alcohols. They are commonly referred to as "surgical alcohol". Used to disinfect the skin before injections are given, often along with iodine ([tincture of iodine](#)) or some [cationic surfactants](#) (benzalkonium chloride 0.05 - 0.5%, chlorhexidine 0.2 - 4.0% or octenidine dihydrochloride 0.1 - 2.0%).

- [Quaternary ammonium compounds](#)
They include the chemicals [benzalkonium chloride](#) (BAC), [cetyl trimethylammonium bromide](#) (CTMB), [cetylpyridinium chloride](#) (Cetrim), [cetylpyridinium chloride](#) (CPC) and [benzethonium chloride](#) (BZT). Benzalkonium chloride is used in some pre-operative skin disinfectants (conc. 0.05 - 0.5%) and antiseptic towels. The antimicrobial activity of Quats is inactivated by [anionic surfactants](#), such as soaps. Related disinfectants include [chlorhexidine](#) and octenidine.
- [Boric acid](#)
Used in suppositories to treat [yeast](#) infections of the [vagina](#), in eyewashes, and as an antiviral to shorten the duration of [cold sore](#) attacks. Put into creams for burns. Also common in trace amounts in eye contact solution. Though it is popularly known as an antiseptic, it is in reality only a soothing fluid, and bacteria will flourish comfortably in contact with it.
- [Chlorhexidine Gluconate](#)
A biguanidine derivative, used in concentrations of 0.5 - 4.0% alone or in lower concentrations in combination with other compounds, such as alcohols. Used as a skin antiseptic and to treat inflammation of the gums ([gingivitis](#)). The microbicidal action is somewhat slow.

[Hydrogen peroxide](#)

Used as a 6% (20Vols) solution to clean and deodorise wounds and [ulcers](#). More common 1% or 2% solutions of hydrogen peroxide have been used in household first aid for scrapes, etc. However, even this less potent form is no longer recommended for typical wound care as the strong oxidization causes scar formation and increases healing time. Gentle washing with mild soap and water or rinsing a scrape with sterile saline is a better practice.

- [Iodine](#)
Usually used in an [alcoholic](#) solution (called [tincture of iodine](#)) or as [Lugol's iodine](#) solution as a pre- and post-operative antiseptic. No longer recommended to disinfect minor wounds because it induces scar tissue formation and increases healing time. Gentle washing with mild soap and water or rinsing a scrape with sterile saline is a better practice. Novel iodine antiseptics containing iodopovidone/PVP-I (an [iodophor](#), complex of povidone, a water-soluble [polymer](#), with triiodide anions I_3^- , containing about 10% of active iodine, with the commercial name Betadine) are far better tolerated, don't affect wound healing

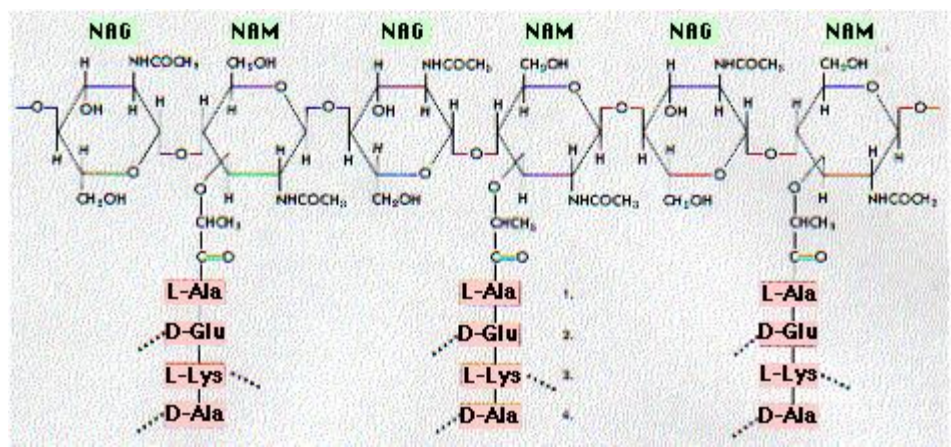
negatively and leave a depot of active iodine, creating the so-called "remanent," or persistent, effect. The great advantage of iodine antiseptics is the widest scope of antimicrobial activity, killing all principal pathogens and given enough time even [spores](#), which are considered to be the most difficult form of microorganisms to be inactivated by disinfectants and antiseptics.

- [Mercurochrome](#)
Not recognized as safe and effective by the U.S. [Food and Drug Administration](#) (FDA) due to concerns about its [mercury](#) content. Another obsolete organomercury antiseptics include bis-(ferylmercury) monohydrogenborate (Famosept).
- [Phenol](#) (carbolic acid) compounds
Phenol is germicidal in strong solution, inhibitory in weaker ones. Used as a "scrub" for pre-operative hand cleansing. Used in the form of a powder as an antiseptic baby powder, where it is dusted onto the belly button as it heals. Also used in [mouthwashes](#) and throat lozenges, where it has a methadone-like [painkilling](#) effect as well as an antiseptic one. Example: [TCP](#). Other phenolic antiseptics include historically important, but today rarely used (sometimes in dental surgery) [thymol](#), today obsolete [hexachlorophene](#), still used [triclosan](#) and sodium 3,5-dibromo-4-hydroxybenzenesulfonate (Dibromol).
- [Sodium chloride](#)
Used as a general cleanser. Also used as an antiseptic mouthwash. Only a weak antiseptic effect, due to [hyperosmolality](#) of the solution above 0.9%.
- [Sodium hypochlorite](#)
Used in the past, diluted, neutralised and combined with [potassium permanganate](#) in the Daquin's solution. Nowadays used only as disinfectant.

How Antibiotics act.

Antibiotics attack a metabolic pathway found in the bacterium but not in the host. This is not an insurmountable problem for bacterial pathogens because they differ in many respects from eukaryotes.

Thus penicillins (beta-lactams) work by interfering with the synthesis of the bacterial cell wall — a structure that is not found in eukaryotes. The walls of



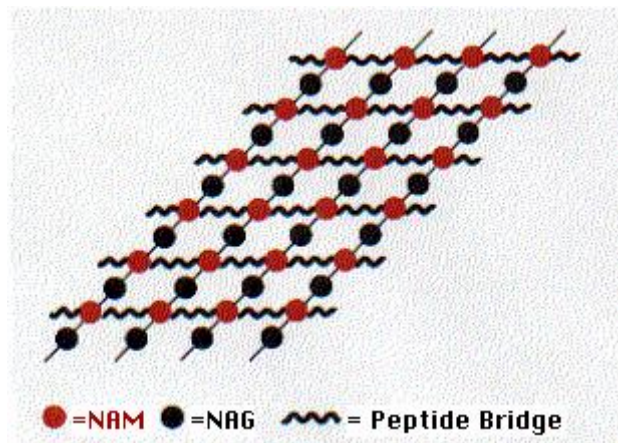
bacteria are made of a complex polymeric material called peptidoglycan. It contains both amino acids and amino sugars. The amino sugars are of two kinds

- N-acetylglucosamine (NAG) and its close relative
- N-acetylmuramic acid (NAM).

These two form a linear polymer of NAG alternating with NAM. They are linked by a glycosidic bond between the #1 and #4 carbons (this is the linkage attacked by lysozyme) and are oriented in the same way they are in cellulose. Side chains containing 4 or 5 amino acids are attached to each NAM. These form covalent bonds with amino acids in adjacent chains. The bonds may

- be direct to the next chain or
- include additional peptide cross bridges (e.g., 5 glycine residues) which
- extend to chains in the same plane (shown here) as well as to chains above and below.

This elaborate, covalently cross-linked structure provides the great strength of the cell wall. It also leads to the remarkable conclusion that the bacterial cell wall meets the definition of a single molecule!



The beta-lactam antibiotics bind to and inhibit enzymes needed for the synthesis of the peptidoglycan wall. While they have little effect on resting bacteria, they are lethal to dividing bacteria as defective walls cannot protect the organism from bursting in hypotonic surroundings.

The **aminoglycosides** bind to the **30S** subunit of the bacterial ribosome, because the bacterial ribosome differs in several ways from the eukaryotic ribosome and thus interferes with the formation of the [initiation complex](#), causing misreading of the mRNA.

Tetracyclines also bind to the **30S** subunit of the bacterial ribosome. They prevent the transfer of activated amino acids to the ribosome so protein synthesis is halted.

The **fluoroquinolones** block the action of two bacterial topoisomerases — enzymes that relieve the coils that form in DNA when the helix is being opened in preparation for replication or transcription or repair.

The mode of action of Sulfonamides is a bit different. Both bacteria and their human hosts require folic acid for nucleic acid synthesis (it is converted into [prunes](#) and [thymidine](#)) as well as protein synthesis (precursor of the amino acids [methionine](#) and [glycine](#)). However, bacteria **synthesize** their folic acid starting with **para-aminobenzoic acid (PABA)**, while we must ingest our folic acid already formed; that is, for us it is a [vitamin](#).

Sulfanilamide, and the other sulfa drugs, are analogs of PABA; they compete with PABA and, when chosen, block the synthesis of folic acid. Mammals ignore PABA and its analogs and thus can tolerate sulfa drugs.

Production of antibiotics

Since the first pioneering efforts of [Florey](#) and [Chain](#) in 1939, the importance of antibiotics to [medicine](#) has led to much research into discovering and producing them. The process of production usually involves screening of wide ranges of microorganisms, testing and modification. Production is carried out using [fermentation](#); a process that is important in anaerobic conditions when there is no oxidative phosphorylation to maintain the production of [adenosine triphosphate](#) (ATP) by [glycolysis](#)