PHARMACEUTICAL CHEMISTRY

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PHARMACEUTICAL CHEMISTRY

UNIT-I

INTRODUCTION

Pharmaceutical chemistry is the study of drugs, and it involves drug development. This includes drug discovery, delivery, absorption, metabolism, and more. There are elements of biomedical analysis, pharmacology, pharmacokinetics, and pharmacodynamics.

Pharmaceutical chemistry involves cures and remedies for disease, analytical techniques, pharmacology, metabolism, quality assurance, and drug chemistry.

Terminology in Pharmaceutical chemistry

Drug

A **drug** is any substance that causes a change in an organism's physiology or psychology when consumed.

Drugs are typically distinguished from food and substance that provide nutritional support.

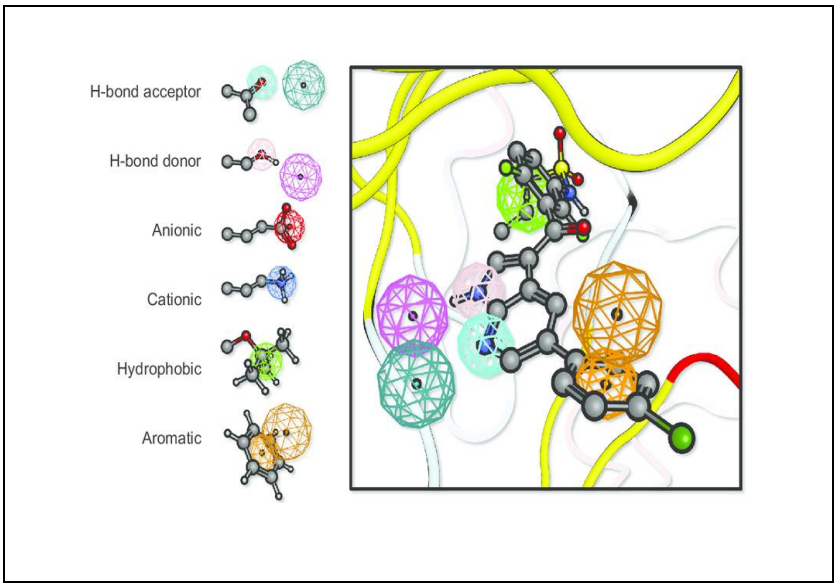
Consumption of drugs can be via inhalation, injection, smoking, ingestion, absorption via a patch on the skin, or dissolution under the tongue.

In pharmacology, a drug is a chemical substance, typically of known structure, which, when administered to a living organism, produces a biological effect. A pharmaceutical drug, also called a medication or medicine.

"Drug is a chemical substance used to treat, cure, prevent, or diagnose a disease or to promote well-being". Traditionally drugs were obtained through extraction from medicinal plants, but more recently also by organic synthesis.

Pharmacophore

The physiological activity of drugs is due to the presence of certain functional groups or structural units. These are called as pharmacophores. A part of a molecular structure that is responsible for a particular biological or pharmacological interaction that it undergoes.



IUPAC defines a Pharmacophore is an ensemble of steric, electrostatic and hydrophobic properties which is essential for optimal Supramolecular interactions with a biological receptor, to modulate or inhibit a biological effect.

Pharmacology

Pharmacology is a branch of medicine and pharmaceutical sciences which is concerned with the study of drug or medication action.

A drug can be broadly defined as any man-made, natural, or endogenous (from within the body) molecule which exerts a biochemical or physiological effect on the cell, tissue, organ, or organism.

More specifically, it is the study of the interactions that occur between a living organism and chemicals that affect normal or abnormal biochemical function.

The field encompasses drug composition and properties, synthesis and drug design, molecular and cellular mechanisms, organ/systems mechanisms, signal transduction/cellular communication, molecular diagnostics, interactions, chemical biology, therapy, and medical applications and antipathogenic capabilities.

The two main areas of pharmacology are **pharmacodynamics** and **pharmacokinetics.** Pharmacodynamics studies the effects of a drug on biological systems, and pharmacokinetics studies the effects of biological systems on a drug.

In broad terms, pharmacodynamics discusses the chemicals with biological receptors, and pharmacokinetics discusses the absorption, distribution, metabolism, and excretion (ADME) of chemicals from the biological systems.

Pharmacopoeia

Pharmacopoeia is an official code, containing a selected list of established drugs and medicinal preparations with the description of their physical properties and tests for their purity and potency. It defines the standards which any preparation must meet and their average doses for any individual. Few well-known pharmacopoeias are:

- Indian Pharmacopoeia (IP)
- British Pharmacopoeia (BP)
- United States Pharmacopoeia (USP)
- European Pharmacopoeia(EP)

Bacteria

Bacteria are prokaryotic microorganisms. “Bacteria” is a plural form of “Bacterium”.

Bacteria are Single-celled microorganisms that can exist either as independent (free-living) organisms or as parasites (dependent on another organism for life).

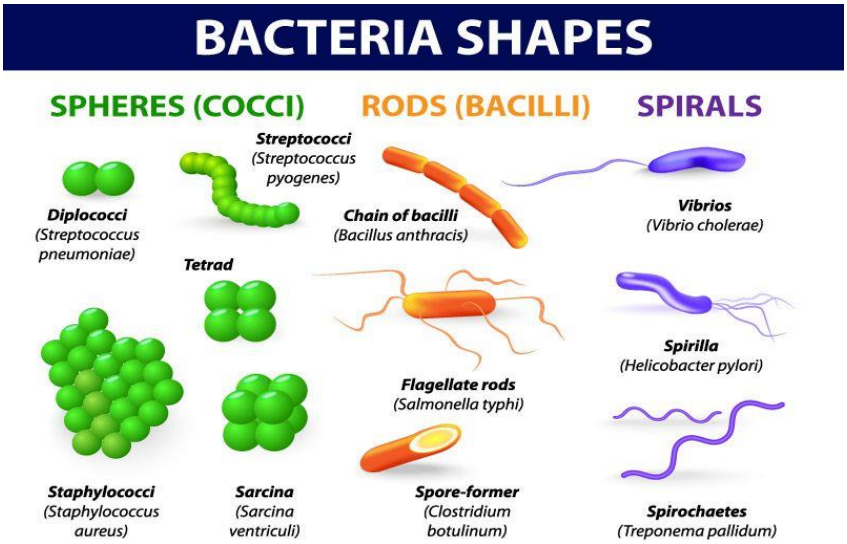
They have cell walls but lack organelles and an organized nucleus, including some which can cause disease.

While several bacterial species are pathogenic (capable to causing diseases), most are non-infectious, and many have critical roles in decay, fermentation, nutrient recycling and nitrogen fixation.

Bacteria are usually classified as gram-positive and gram-negative based on basic microbiological staining procedure called the gram stain.

There are three basic shapes of bacteria:

- Spheres (Coccus) : Streptococcus group
- Rods (Bacillus) : Bacillus anthracis
- Spirals : Spirillum



Virus

A **virus** is a submicroscopic infectious agent that replicates only inside the living cells of an organism.

Viruses can infect all types of life forms, from animals and plants to microorganisms, including bacteria and archaea.

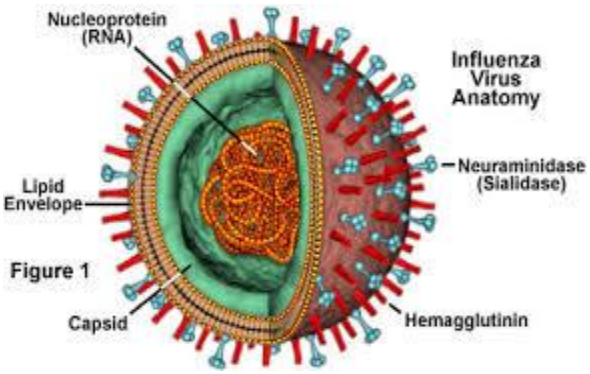


Figure 1

Since Dmitri Ivanovsky's 1892 article describing a non-bacterial pathogen infecting tobacco plants, and the discovery of the tobacco mosaic virus by Martinus Beijerinck in 1898, more than 6,000 virus species have been described in detail, of the millions of types of viruses in the environment. Viruses are found in almost every ecosystem on Earth and are the most numerous type of biological entity.

The Latin word virus means venom or poison.

The study of viruses is known as virology, a subspeciality of microbiology.

Virus are smaller than bacteria, they range in size between 20-300 nanometer.

Virus are obligate intracellular parasites consist of nucleic acid surrounded by a protein coat. Some virus are have additional lipoprotein envelope.

Viruses contain only one type of nucleic acid, either DNA or RNA, but never both.

Example

- DNA viruses: Hepatitis B, herpesvirus, poxvirus etc.,
- RNA viruses: Influenza, Sars, HIV, Covid-19 etc.,

Viruses spread in many ways. One transmission pathway is through disease-bearing organisms known as vectors: for example, viruses are often transmitted from plant to plant by insects that feed on plant sap, such as aphids; and viruses in animals can be carried by blood-sucking insects. Influenza viruses are spread by coughing and sneezing. Norovirus and rotavirus, common causes of viral gastroenteritis, are transmitted by the faecal–oral route, passed by hand-to-mouth contact or in food or water. The infectious dose of norovirus required to produce infection in humans is less than 100 particles. HIV is one of several viruses transmitted through sexual contact and by exposure to infected blood.

Chemotheraphy

Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cells in your body.

Chemotherapy is most often used to treat cancer, since cancer cells grow and multiply much more quickly than most cells in the body. Many different chemotherapy drugs are available. Chemotherapy drugs can be used alone or in combination to treat a wide variety of cancers.

Though chemotherapy is an effective way to treat many types of cancer, chemotherapy treatment also carries a risk of side effects. Some chemotherapy side effects are mild and treatable, while others can cause serious complications.

Vaccine

A vaccine is a biological preparation that provides active acquired immunity to a particular infectious disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from **weakened or killed forms of the microbe**, its toxins, or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as a threat, destroy it, and to further recognize and destroy any of the microorganisms associated with that agent that it may encounter in the future.

The administration of vaccines is called **vaccination**. Vaccination is the most effective method of preventing infectious diseases; widespread immunity due to vaccination is largely responsible for the worldwide eradication of smallpox and the restriction of diseases such as polio, measles, and tetanus from much of the world. The effectiveness of vaccination has been widely studied and verified; for example, vaccines that have proven effective include the influenza vaccine, the HPV vaccine, and the chicken pox vaccine. The World Health Organization (WHO) reports that licensed vaccines are currently available for twenty-five different preventable infections.

The terms vaccine and vaccination are derived from **Variolae vaccinae** (smallpox of the cow), the term devised by **Edward Jenner** to denote **cowpox**. He used it in 1798 in the long title of his Inquiry into the Variolae vaccinae Known as the Cow Pox, in which he described the protective effect of cowpox against smallpox. In 1881, to honor Jenner, Louis Pasteur proposed that the terms should be extended to cover the new protective inoculations then being developed.

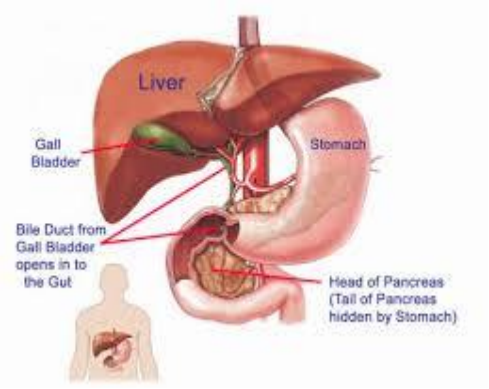
JAUNDICE

Jaundice is a term used to describe the yellowing of the skin and the whites of the eyes. Jaundice comes from the French word *jaune,* which means yellow.

Jaundice is the yellow colouration of the skin, the mucous membranes or the eyes caused by high level of the chemical substance called bilirubin in the blood and body's tissues. The colour

of the skin and sclera vary depending on the level of bilirubin. When the bilirubin level is slightly elevated they are yellowish. When the bilirubin level is high, they tend to be brown.

CAUSES



Bilirubin comes from red blood cells. When red blood cells get old, they are destroyed. Haemoglobin, the iron containing chemical in red blood cells that carries oxygen, is released from the destroyed red blood cells after the iron it contains is removed. The chemical that remains in the blood after the iron is removed becomes bilirubin.

One of the functions of liver is to produce and secrete bile into the intestine to help digest dietary fat. Another function is to remove toxic chemicals or waste products from the blood.

After the bilirubin has entered the liver cells, the cells conjugate to the bilirubin, and then secrete bilirubin-glucuronic acid complex into bile. The complex that is secreted in bile is called conjugated bilirubin. The conjugated bilirubin is eliminated in the faeces. Jaundice occurs when there is:

- If red blood cells broke down too early, the spleen gets overloaded and hence too much bilirubin is produced to be handled by the liver. Unprocessed bilirubin accumulates in the bloodstream and eventually the skin and eyes looks yellow. This condition is called hemolytic anemia. At times this condition is inherited. Hemolytic anemia may also occur as a side-effect of certain drugs.

- Viruses including Hepatitis A, chronic Hepatitis B and C and Epstein-Barr virus infection.

- Sometimes the trouble is in the liver cells. If there is a faulty uptake, processing or excretion of bilirubin it will result in an accumulation of bilirubin in the bloodstream. Newborn babies can be temporarily jaundiced because of lack of mature enzymes needed

to process bilirubin. In adults, alcoholism is a common cause of damage to liver cells. Other toxins and certain drugs can also cause acute damage to the liver.

- A blockage in the bile duct can also result in a build-up of fully processed bilirubin. This can spill over into the urine and cause it to become very dark. The blockage is most commonly caused by
    - Gallstones
    - Inflammation of the gallbladder
    - Gallbladder cancer
    - Pancreatic tumor

Classification

Jaundice is classified into three categories, depending on which part of the physiological mechanism the pathology affects. The three categories are:

Pre-hepatic jaundice: Pre hepatic jaundice is due to increased rate of haemolysis (breakdown of RBCs). Hence it causes an unconjugated hyperbilirubinaemia that remains in the blood stream to cause the jaundice.Causes of haemolysis include:

- Malaria
- Sickle cell anemia
- Thalassaemia
- Gilbert syndrome

Hepatocellular jaundice: Hepato cellular jaundice can be due to any infection in the liver. It can be due to infection or exposure to a harmful substance, such as alcohol, disrupts the liver's ability to process bilirubin.

Post hepatic jaundice: Post-hepatic jaundice, is also called as obstructive jaundice, is caused by an interruption to the drainage of bile in the biliary system. The most common cause is due to gallstone in the common bile duct or due to pancreatic cancer. Some underlying conditions that may cause jaundice are:

- **Acute inflammation of the liver** – May impair the ability of the liver to conjugate and secrete bilirubin, resulting in a buildup of bilirubin.
- **Inflammation of the bile duct** – May prevent the secretion of bile and removal of bilirubin, causing jaundice.
- **Obstruction of the bile duct** – Prevents the liver from disposing of bilirubin, which results in hyperbilirubinemia.
- **Hemolytic anemia** – Production of bilirubin increases when large quantities of erythrocytes are broken down.
- **Gilbert's syndrome** – An inherited condition that impairs the ability of enzymes (biomolecules that provoke chemical reactions between substances) to process the excretion of bile.
- **Cholestasis**– A condition in which the flow of bile from the liver is interrupted. The bile containing conjugated bilirubin remains in the liver instead of being excreted.

Symptoms

The main symptoms of jaundice are:

- Fever
- Weight loss
- Yellow discoloration of the eyes and of the skin
- Pale coloured stools (faeces)
- Dark coloured urine
- Abdominal pain

Diagnosis

Urine test: It is used to measure levels of a substance called urobilinogen. Urobilinogen is produced when bacteria break down bilirubin inside the digestive system.

Blood tests: Blood tests include blood levels of enzymes found primarily from the liver, such as the aminotransferases (ALT, AST), and alkaline phosphatase (ALP), bilirubin (which causes the jaundice), and protein levels, specifically, total protein and albumin.
Other primary lab tests for liver function include gamma glutamyl transpeptidase (GGT) and prothrombin time (PT).

Treatment

There's no treatment for jaundice as such, but disease can be managed by managing symptoms and causes of jaundice. Jaundice treatment targets the causes rather than the jaundice symptoms.

- Anemia-induced jaundice may be treated by boosting the amount of iron in the body by either taking iron supplements or eating more iron-rich foods.
- Hepatitis-induced jaundice requires antiviral or steroid medications.
- Doctors can treat obstruction-induced jaundice by surgically removing the obstruction.
- If the jaundice has been caused by use of a medication, treatment for involves changing to an alternative medication.

Prevention

It's not possible to prevent all cases of jaundice because it can be caused by a wide range of conditions or circumstances.

However, by taking certain precautions risk of developing jaundice can be minimised. These include:

- Ensuring not to exceed the recommended daily amount (RDA) for alcohol consumption.
- Maintaining a healthy weight for height and build.
- Vaccination against hepatitis A and hepatitis B.
- Avoid high-risk behaviours such as intravenous drug use or unprotected intercourse.
- Avoid potentially contaminated food/water and maintain good hygiene
- Avoid medications and toxins which can cause hemolysis or directly damage the liver.

Cholera

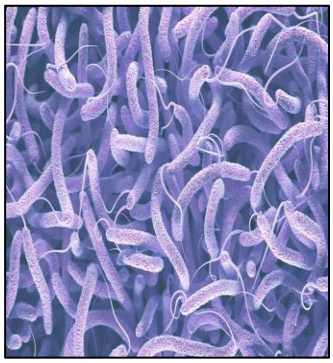
Cholera is an infectious disease that causes severe watery diarrhea, which can lead to dehydration and even death if untreated. It is caused by eating food or drinking water contaminated with a bacterium called ***Vibrio cholera.***

Raw seafood may be the source of infections in areas where cholera is prevalent. A series of six pandemics of cholera, originating in the Bengal basin, ravaged the world in the 19th and early 20th centuries killing thousands of people. Cholera is endemic in India and South-East Asia.

Causes of cholera

A bacterium called Vibrio cholera causes cholera, is usually found in food or water contaminated by feces from a person with the infection. The deadly effects of the disease are the result of a toxin causes the body to secrete enormous amounts of water, leading to diarrhea and a rapid loss of fluids and salts (electrolytes).

Contaminated water supplies are the main source of cholera infection.



vibrio cholera bacterium (SEM image)

The bacterium can be found in:

- Surface water: The contamination usually occurs when untreated sewage is released in to waterways affecting the water supply.
- Foods and drinks sold by street vendors
- Vegetables grown with water containing human wastes
- Raw or undercooked fish and seafood caught in waters polluted with sewage
- The resulting diarrhoea allows bacteria to spread to other people under poor sanitary.

Symptoms

Symptoms of cholera can begin as soon as a few hours or as long as five days after infection. Often, symptoms are mild. But sometimes they are very serious. About one in 20 people infected have severe watery diarrhoea accompanied by vomiting, which can quickly lead to dehydration. Although many infected people may have minimal or no symptoms, they can still contribute to spread of the infection. The cholera toxin interacts with G proteins and cyclic AMP in the intestinal lining to open ion channels. The loss of potassium ion may result in cardiac complications and circulatory failure,

The common symptoms include:

- Rapid heart rate
- Loss of skin elasticity (dry skin)
- Dry mucous membranes, including the inside of the mouth, throat, nose, and eyelids
- Low blood pressure
- Thirst
- Muscle cramps
- Diarrhoea has a fishy odur
- Tiredness
- Low urine output
- Abdominal cramps
- Nausea
- Vomiting

However the symptoms can vary from mild to severe and person to person.

If not treated, dehydration can lead to shock and death in a matter of hours.

Treatment

There is a vaccine for cholera. Both the CDC and the World Health Organization have specific guidelines for who should be given this vaccine.

- Rehydration therapy: cholera can be treated by adequate administration of oral rehydration salts (ORS) to replace the lost fluids and salts.
- Severely dehydrated persons should be given ORS intravenously. The world Health Organization (WHO) has developed an oral rehydration solution that is cheaper and easier to use than the typical intravenous fluid. This solution is now being used internationally.
- Antibiotic treatment: Use antibiotics like tetracycline, cotrimoxazole, erythromycin, doxycyclin, choramphenicol and furazolidone are administered to reduce fluid requirements and duration of illness, is indicated for severe case of cholera
- Zinc treatment has also been show to help improve cholera symptoms in children.

Prevention

Simple solution is usually sufficient to stop an epidemic. Prevention of cholera is odependent on access to safe water, adequate sanitation, and basic hygienic needs.

Malaria

Malaria is a disease caused by parasite. The parasite is transmitted to humans through the bites of infected mosquitoes. People who have malaria usually feel very sick, with a high fever and shaking chills.

Causes

Malaria is a life-threatening disease. It's typically transmitted through the bite of an infected *Anopheles* mosquito. Infected mosquitoes carry the *Plasmodium* parasite. Four spices of plasmodium can produce the disease in its various forms:

- Plasmodium falciparum
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malariae

P.falciparum is the most widespread and dangerous of the four. When left untreated it can lead to fatal cerbal malaria.

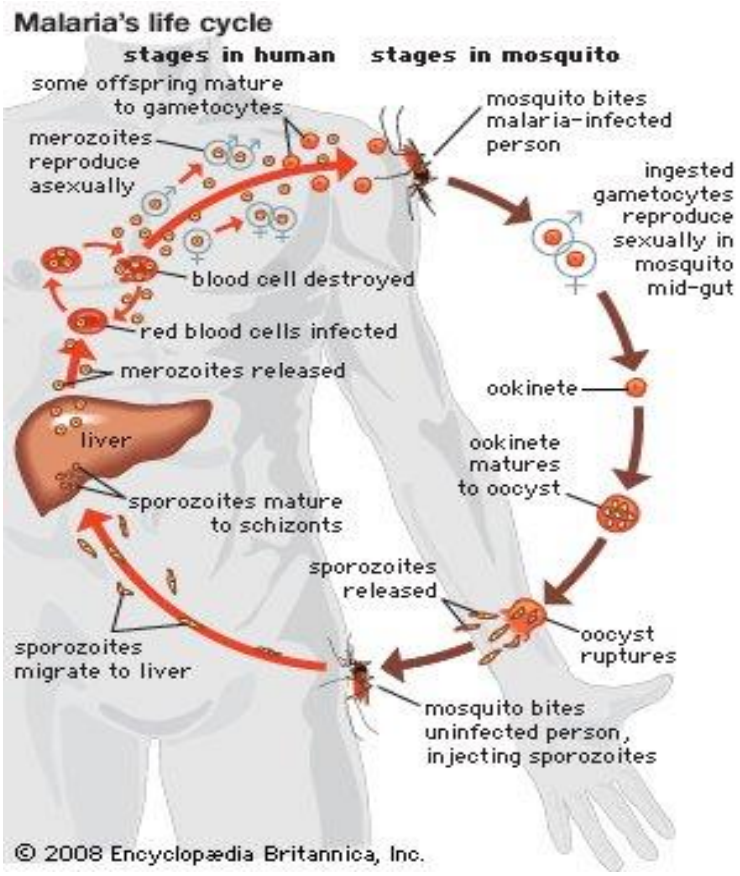
When this mosquito bites you, the parasite is released into your bloodstream. Once the parasites are inside your body, they travel to the liver, where they mature. After several days, the mature parasites enter the bloodstream and begin to infect red blood cells.

Within 48 to 72 hours, the parasites inside the red blood cells multiply, causing the infected cells to burst open.

The parasites continue to infect red blood cells, resulting in symptoms that occur in cycles that last two to three days at a time.

Mosquito transmission cycle

- The cycle begins when a mosquito becomes infected by feeding on a person`s blood who has malaria
- **Transmission of parasite:** When the infected mosquito bites again, the parasites are injected into the person being bitten, spreading the infection.
- **In the liver.** Once the parasites enter a human, the parasites multiply in the liver. Within an average of 2 to 4 weeks, they mature and are released into the blood.
- **Into the bloodstream.** When the parasites mature, they leave the liver and infect red blood cells and multiply again. Eventually, the RBCs rupture releasing new parasites to enter new RBCs repeating the cycle. This is when people typically develop malaria symptoms within 48 hours.



Symptoms

The symptoms of malaria may be mild at first and are similar to the flu, making them difficult to diagnose. A person with malaria may experience the following symptoms.

- The classical malarial fever has three stages.

  Cold stage (shivering) lasting for 2 hours,

  Host stage lasting for 3-4 hours,

  Sweating lasting for 2-4 hours.

These symptoms occur at regular intervals, i.e., they show periodicity

- Headache
- Cough
- Abdominal pain
- Nausea and vomiting
- Muscle pain and fatigue
- Black water fever

- Malaria caused by the P.falciparum parasite is the only type known to be life threatening P.falicparum malaria can lead to:
    - Liver failure
    - Kidney failure
    - Fluid in the lungs
    - Convulsions
    - Coma

Diagnosis

Malaria is diagnosed by staining blood smears with Giemsa and examining through microscope. This test helped to found parasite type and level in patient blood.

Treatment

Malaria can be a severe, potentially fatal disease (especially when caused by *Plasmodium falciparum*), and treatment should be initiated as soon as possible. Which drug regimen to treat a patient with malaria depends on the clinical status of the patient, the type (species) of the infecting parasite, the area where the infection was acquired and its drug-resistance status, pregnancy status, and finally history of drug allergies, or other medications taken by the patient.

The most common antimalarial drugs include:

- **Artemisinin-based combination therapies (ACTs).** ACTs are, in many cases, the first line treatment for malaria. There are several different types of ACTs. Examples include artemether-lumefantrine (Coartem) and artesunate-amodiaquine. Each ACT is a combination of two or more drugs that work against the malaria parasite in different ways.
- **Chloroquine phosphate.** Chloroquine is the preferred treatment for any parasite that is sensitive to the drug. But in many parts of the world, the parasites that cause malaria are resistant to chloroquine, and the drug is no longer an effective treatment.

Other common antimalarial drugs include:

- ✓ Combination of atovaquone and proguanil (Malarone)
- ✓ Quinine sulfate (Qualaquin) with doxycycline (Vibramycin, Monodox, others)
- ✓ Mefloquine
- ✓ Primaquine phosphate

Prevention

Transmission of malaria can be barred by

- Preventing proliferation of mosquitoes; water should not be allowed to stagnant since stagnant waters are breeding grounds for mosquitoes.
- Preventing mosquito bites by using mosquito repellents, bed nets, and clothing that covers most of the body.
- Chemoprophylaxis (preventive medications).

Filaria

Filariasis is a parasitic disease caused by an infection with roundworms of the Filarioidea type. These are spread by blood-feeding insects such as black flies and mosquitoes. They belong to the group of diseases called helminthiases.

Eight known filarial worms have humans as a definitive host. These are divided into three groups according to the part of the body they affect:

- Lymphatic filariasis is caused by the worms *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*. These worms occupy the lymphatic system, including the lymph nodes; in chronic cases, these worms lead to the syndrome of *elephantiasis*.
- Subcutaneous filariasis is caused by *Loa loa* (the eye worm), *Mansonella streptocerca*, and *Onchocerca volvulus*. These worms occupy the layer just under the skin. *L. loa* causes *Loa loa* filariasis, while *O. volvulus* causes river blindness.
- Serous cavity filariasis is caused by the worms *Mansonella perstans* and *Mansonella ozzardi*, which occupy the serous cavity of the abdomen. *Dirofilaria immitis*, the dog heartworm, rarely infects humans.

The adult worms, which usually stay in one tissue, release early larval forms known as microfilariae into the person's blood. These circulating microfilariae can be taken up during a blood meal by an insect vector; in the vector, they develop into infective larvae that can be spread to another person.

LYMPHATIC FILARIASIS (Elephantiasis)

This disease is caused by the nematode worm, either ***Wuchereria bancrofti*** or ***Brugia malayi*** and is transmitted by mosquito species Culex quinquefasciatus and Mansonia annulifera/M.uniformis respectively.

The disease generally presents with the symptoms like swelling of legs, and hydrocele and can cause a raft of societal stigma.

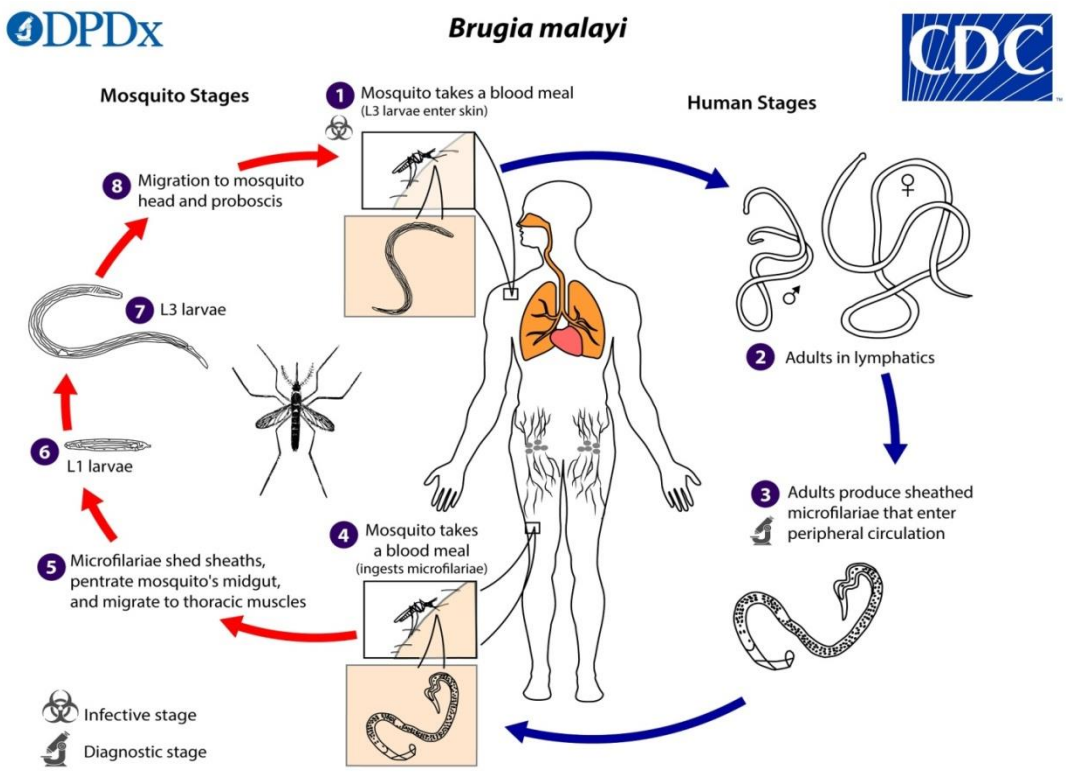
Lymphatic Filariasis (LF) is commonly known as elephantiasis. It is a disfiguring and disabling disease, which is generally aquired in childhood. In the early stages,though there are either no symptoms or non-specific symptoms, the lymphatic system is damaged. This stage can last for several years. Infected persons sustain the transmission of the disease. The long term physical consequences are painful swollen limbs (lymphoedema or elephantiasis). Hydrocele in males is also common in endemic areas.

Causes

Most cases of filariasis are caused by the parasite known as Wuchereria bancrofti. Culex, Aedes and Anopheles mosquitoes serve as vector for W.bancrofti in transmission of the disease. Another parasite called Brugia malayi also causes filariasis is transmitted by the vector Mansonia and Anopheles mosquitoes.

When an infected mosquito bites a healthy person, the larvae called microfilariae move into the lymphatics and lymph nodes. Here, they develop into adult worms and may persist for years.

The adult parasite, in turn, produces more microfilariae. These microfilariae circulate in the peripheral blood usually in the night, and are sucked by the mosquitoes during a bite. The same cycle is then repeated in another healthy individual.



Symptoms

- Lymphatic filariasis infection involves asymptomatic, acute, and chronic conditions. The majority of infections are asymptomatic, showing no external signs of infection, although their blood is positive for microfilaria. This stage may lasts for months.
- Acute episodes of local inflammation involving skin, lymph nodes and lymphatic vessels.
- Chronic condition shows oedema with thickening of the skin and underlying tissues (the classical symptom of filarasis).
- It usually affects the lower extremities. However, the arms, vulva, breasts and scrotum (causing hydrocele formation) can also be affected.The oedema in the extremities, breast or genital area can result in the part becoming several times its normal size and is due to blockage of the vessels of the lymphatic system.

Diagnosis

Blood sample:

The microfilariae that cause lymphatic filariasis circulate in the blood at night (called nocturnal periodicity). Blood collection should be done at night to coincide with the appearance

of the microfilariae, and a thick smear should be made and stained with Giemsa or hematoxylin and eosin. For increased sensitivity, concentration techniques can be used.

Serological examination:

Serologic techniques provide an alternative to microscopic detection of microfilariae for the diagnosis of lymphatic filariasis. Patients with active filarial infection typically have elevated levels of antifilarial IgG4 in the blood and these can be detected using routine assays.

Treatment

- Administrating medicine to kill circulating larvae and adult worms.
- Soap and water and skin care to prevent secondary infections
- Elevation, exercise and in some cases, pressure bandages to reduce swelling.
- The recommended regimen for treatment of filariasis is mass drug administration (MDA) in which a single dose of two medicines are given together – albendazole (400 mg) with either ivermectin (150-200 mcg/kg) in areas where onchocerciasis (river blindness) is also endemic or diethylcarbamazine citrate (DEC) (6 mg/kg) in areas where onchocerciasis is not endemic. These medicines clear microfilariae from the bloodstream.

Prevention

The best way to prevent lymphatic filariasis is to avoid mosquito bites. The mosquitoes that carry the microscopic worms usually bite between the hours of dusk and dark.

Spraying exposed skin with an mosquito repellent.

First aid

First aid is the first and immediate assistance given to any person suffering from either a minor or serious illness or injury, with care provided to preserve life, prevent the condition from worsening, or to promote recovery.

It includes initial intervention in a serious condition prior to professional medical help being available, such as performing cardiopulmonary resuscitation (CPR) while waiting for an ambulance, as well as the complete treatment of minor conditions, such as applying a plaster to a cut. First aid is generally performed by someone with basic medical training. Mental health first aid is an extension of the concept of first aid to cover mental health, while psychological first aid is used as early treatment of people who are at risk for developing PTSD. Conflict First Aid, focused on preservation and recovery of an individual's social or relationship well-being, is being piloted in Canada.

The basic aims of first aid are :

1. To save life.
2. To protect the casualty from getting more harm.
3. To reduce pain and priorities of Casualty Treatment.

There are many situations which may require first aid

Immediate Requirement :

Critical four minutes: One of the most common causes of a road accident death is due to loss of oxygen supply. This is mostly caused by a block airway. Normally it takes less than four minutes for a blocked airway to cause death.

The 'golden hour': The first hour after the Trauma is called the 'golden hour'. If proper first aid is given, road accident victims have a greater chance of survival and a reduction in the severity of their injuries.

In case of Wound :

The job of first-aider is to remove or reduce the problems that hamper healing such as dirt, infection, movement, etc. Leave the wound undisturbed. Clean the wound by washing them with running water. If there are splinters, thorns and pieces of glass inside the wound remove them with a pair of tweezers so as to avoid infection.

In case of Profuse bleeding

The easiest way to stop bleeding is to apply direct pressure on the wound. This can be done with any clean folded cloth. Lean on the wound with the heel of the hand instead of your fingers.

In case of a Fracture :

In case of a fracture do not apply direct pressure; instead use a splint, combined with as gentle pressure bandage. It is safer not to give the patient anything to eat and drink. This is to protect the patient from vomiting in case he needs anesthesia and surgery, or has a head injury.

If the wound on the arm or the leg is bleeding profusely, it can be raised. This reduces the blood flow to the wounded area.

In case of Chest or Abdomen injury :

In abdominal wounds the intestines may come out. The only thing you can do as first-aider is to cover the wound with a very wet clean cloth and get the patient quickly to a hospital. The wet cloth will keep the intestine from drying out, and will stick to the intestine.

In case of Chest or Abdomen injury :

Open wounds of the chest could be sucking in the air, making it hard for the patient to breathe. Covering of the wound with a piece of polythene and putting a bandage on the top of this may help to reduce air being sucked into the chest. Get the patient quickly to hospital

In case part of a Limb is cut off :

If a part of the limb has been cut off it may be possible to reattach it to the body. Put it inside a clean polythene bag and place this bag in another bag with cold water. If you can easily get ice put some in the water to keep it cool. Make sure that the limb does not get soaked in water. If nothing else is available, carry the amputated part in a clean cloth quickly to hospital.

In large crush injuries or in amputation avoid washing the wounds, as it will lead to more blood loss. Just cover the wound with clean cloth and tie a pressure bandage quickly. If possible keep the limb raised. Avoid using raw cotton wool to cover a wound as it gets stuck to the wound, and is difficult to remove and delay healing.

In case of an Eye Wound :

Do not attempt any cleaning or washing of an open eye injury. Cover the eye with a clean soft cloth; place a stiff covering on top to prevent any pressure coming on the eye. This is important because the contents can be squeezed out even through a very small wound.

In case Bleeding from Nose :

Bleeding from nose could also mean a head injury. If the patient is conscious and can sit up, ask him to pinch his nose and breathe through his mouth. If he can lean forward, then that could prevent blood from going to his wind pipe choking him. If the patient is unconscious he should lie with the face to one side, for the blood to come out easily, so that there is no choking.

In case of Bleeding from Ear :

Bleeding from ears mean either injury to the ear alone, or serious head injury. Avoid putting anything in the ears to stop bleeding as this could further damage the eardrum. Gets the patient to lie down with the injured ear facing down.

In case of Injuries to Muscles, Bones and Joints :

When muscle joints or bones get injured, blood collects over the area, and a swelling appears. You can reduce the swelling by bringing down the bleeding. Apply cold water or ice packs if available. It reduces local blood flow and this brings down the internal bleeding and swelling. But remember not to keep ice packs on more than ten minutes at a stretch as this will lead to something like frostbite, and not to place ice directly on skin. Always wrap it in a cloth first. A muscle injury can be made less painful by putting a splint on the injured limb.

In case of Broken Bones and Dislocated Joints :

A fracture or dislocation can be confirmed if there is obvious deformity, abnormal mobility, if the limb cannot be moved at all and if a grating feeling is there. First aid for all fractures and dislocations must aim to reduce movement, which will give relief from pain. Splinting should be done with caution.

Shifting the Injured to the Hospital :

1. Ensure that he is not hurt more.
2. The patient should be carried on firm board of stretcher so spine remains stable.
3. While shifting, the patient's back, neck and airway need to be protected from further injury. So always take help of another person.
4. If the patient is unconscious, gently place a large folded cloth or towel under the neck so that the neck doesn't sag against the ground.
5. The vehicle used to carry the patient to the hospital should have enough space to keep the patient's back straight and the person accompanying should be able to care for and

resuscitate the patients if necessary.

6. During transportation keep a watch on whether the patient's airway is clear, whether the patient is breathing and whether you can feel the pulse in the patient.
7. If there is only one limb injury the patient can be safely taken to hospital on a chair in a sitting position. Take care to splint or protect limb injuries or bleeding.

Antidotes for poisioning

Antidote is Remedy to counteract the effects of a poison or toxin. Administered by mouth, intravenously, or sometimes on the skin, it may work by directly neutralizing the poison; causing an opposite effect in the body; binding to the poison to prevent its absorption, inactivate it, or keep it from fitting a receptor at its site of action; or binding to a receptor to prevent the poison's binding there, blocking its action. Some poisons are not active until converted to a different form in the body; their antidotes interrupt that conversion.

The antidotes for some particular toxins are manufactured by injecting the toxin into an animal in small doses and extracting the resulting antibodies from the host animals' blood. This results in an antivenin that can be used to counteract venom produced by certain species of snakes, spiders, and other venomous animals. Some animal venoms, especially those produced by arthropods (such as certain spiders, scorpions, and bees) are only potentially lethal when they provoke allergic reactions and induce anaphylactic shock; as such, there is no "antidote" for these venoms; however anaphylactic shock can be treated (e.g. with epinephrine).

Some other toxins have no known antidote. For example, the poison aconitine – a highly poisonous alkaloid derived from various aconite species – has no antidote, and as a result, is often fatal if it enters the human body in sufficient quantities.

Treatment should be given immediately and should not be delayed by spending excessive time in attempting to identify the poison. Basic therapeutic principles for the treatments are:

1. Maintenance of Respiration

A clear airway is necessary this can be ensured by removal of dentures, vomits, foreign bodies etc. patient should be turned to one side to prevent tongue falling backwards causing

obstructions to the air passage and to avoid aspiration of vomits and mucus. Oxygen should be given.

2. Inactivation or removal of poison

When a liquid or solid poison is in contact with the patient's body are clothes, these must be removed and washed off to avoid any absorption.

3. Vomiting, gastric aspiration and lavage.

When the poison has been swallowed, conscious patient should be given an emetic i.e. two table spoon of salt to a tumbler of water to induce vomiting.

If the patient is unconscious or if the poison is corrosive like acids or alkalis, vomiting should not be induced. In such case the poison should be neutralized by giving an antidote.

In few cases of poisoning gastric aspiration and lavage is done which is process of draining the fluid from stomach by suction and washing the stomach or rectum by tipid water.

4. Dilution of the poison.

The poison must be diluted by giving large quantities of cold water which will dilute the irritant and lessen irritating effects.

1.3 **Organic pharmaceutical aids**

Pharmaceutical aids-definition

Pharmaceutical aids (pharmaceutical necessity) a substance having slight or no value ther apeutically, but used in the preparation of various pharmaceuticals, including preservatives, solvents, ointment bases, and flavoring, coloring, diluting, emulsifying, and suspending agents.

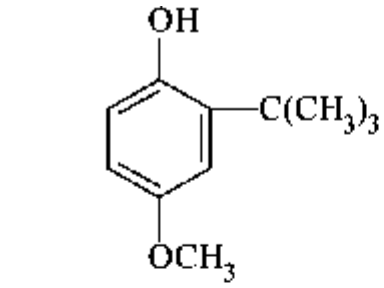
CLASSIFICATION:

It is possible to classify the various pharmaceutical aids into various categories which are given as follows:

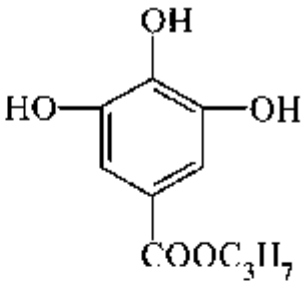
1. Acidifiers and alkalisers.
2. Buffers.
3. Absorbents and adsorbents.
4. Antioxidants and preservatives.
5. Desiccants.
6. Excipients.
7. Suspending agents.
8. Filter aids.
9. Colorants.
10. Tonicity adjusting agents.
11. Solvent and vehicle.
12. Coloring, flavoring and sweetening agents.
13. Ointments and suppository bases.
14. Diluents, binders, disintegrating agents and lubricants

Antioxidants

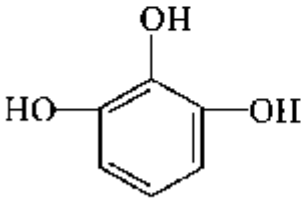
Antioxidants are compounds that inhibit oxidation. Oxidation is a chemical reaction that can produce free radicals, thereby leading to chain reactions that may damage the cells of organisms. Examples: Ascorbic acid (vitamin c), butylated hydroxyanisole (BHA), butylated hydroxytollune (BHT), propylgallate etc



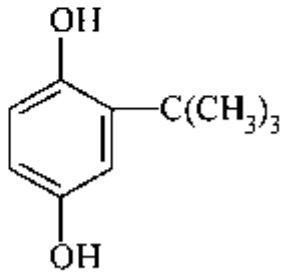
Butylated Hydroxyanisole
(BHA)



Propyl Gallate
(PG)



Pyrogallol
(PY)



tert-Butylatedhydroquinone
(TBHQ)

An antioxidant is a molecule that inhibits the oxidation of other molecules. Oxidation is a chemical reaction involving the loss of electrons or an increase in oxidation state. Oxidation reaction can produce free radicals. In turn, these radicals can start chain reactions. When the chain reaction occurs in a cell, it can cause damage or death to the cell. Antioxidants terminate these chain reactions by removing of free radical intermediates, and inhibit other oxidation reactions.

The following are some of the qualities of an ideal anti-oxidant

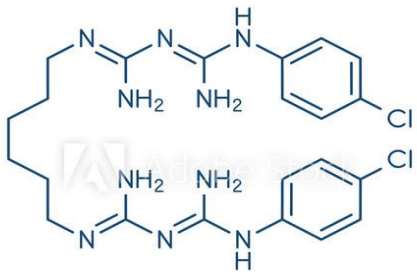
- ✓ It should be readily soluble or dispersible in the medium.
- ✓ It should be effective in low concentration.
- ✓ It should be non-toxic.

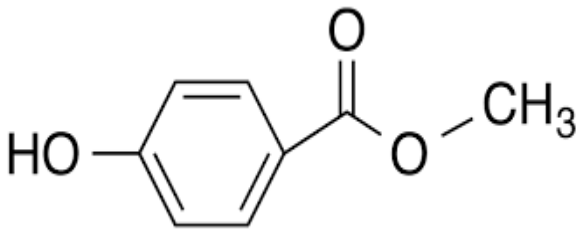
- ✓ It should be compatible with other ingrediants of emulsion.
- ✓ It should be colourless, odourless, and tasteless.

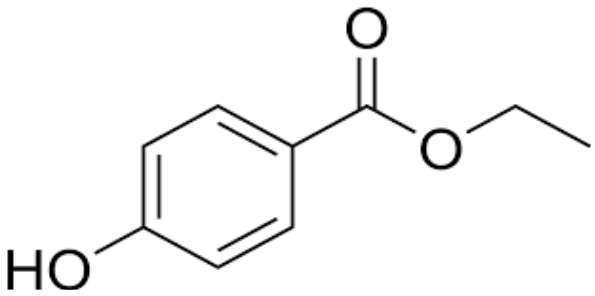
Preservatives

Preservative describes those antimicrobial agents used to protect pharmaceutical preparations.

Examples: ethanol, alcohol, chlorhexidine, benzoic acid, methyl parabenes,







A preservative is a substance or a chemical that is added to products such as food products, beverages, pharmaceutical drugs, paints, biological samples, cosmetics, wood, and many other products to prevent decomposition by microbial growth or by undesirable chemical changes.

In general, preservation is implemented in two modes, chemical and physical. Chemical preservation entails adding chemical compounds to the product. Physical preservation entails processes such as refrigeration or drying. Chemical preservation and physical preservation techniques are sometimes combined.

Preservatives are used in food, cosmetics, pharmaceutical products and many other products.

Need for preservatives

- To protect our drug from microbial attack
- To stabilize product
- To enhance activity and efficiency of drug
- To increase shelf of our product

The following are some of the qualities of Preservatives

- ✓ It should be stable.
- ✓ It should be highly soluble.
- ✓ It should be compatible with other formulation additives.
- ✓ It should be non toxic and non-reactive.
- ✓ It should be odorless and tasteless.
- ✓ Its efficiency should not be decreased by pH.

This occurs most is commonly in antacid suspensions because the pH of antacid suspension is 6-7 at which parabens, benzoates and sorbates are less active.

Parabens are unstable at high pH value so parabenes used effectively when pH is below 8.2.

Preservatives are classified by their source and mechanism of action.

Source:

- o Naturally obtained (lemon, salt)
- o Synthetically prepared (benzoate etc.)

Mechanism of action:

- o Antioxidants (BHA,BHT etc)
- o Antimicrobial agents (phenol, parabenes etc)
- o Chelating agents (EDTA, Citric acid)

Side effect

While choosing preservatives for drug product consideration should be made about concentration, toxicity, selectivity, interaction with formulation etc. some common side effects are:

- Hypersensitivity
- Allergy
- Asthma
- Hyperactivity
- Neurological damage
- Cancer

Some common preservatives used in pharmaceutical preparations with their concentrations:

Substances	**Proportions used**	**Uses**
1. Benzoic acid (IP)	0.1%	It finds use as an antibacterial preservative ingredient of compound Camphor tincture IP.
2. Benzalkonium chloride (USP)	0.01%	It finds use as an antimicrobial preservative
3. Butyl paraben (USP)	0.01% in water 0.15% in oils and creams	It finds use as an antifungal preservative.
4. Centrimide (IP)	0.001%	It finds use as a bactericide.
5. Chlorobutanol (IP, USP)	0.5%	It finds use as an antibacterial preservative.
6. Chlorocresol (IP)	0.1%	It finds use as a bacteriostatic.
7. Cresol (IP)	0.3%	It is used as a disinfectant.
8. Ethyl paraben (USP)	0.5% in water 0.15% in oils and creams	It is used as an antifungal Preservative.
9. Methyl paraben (IP, USP)	0.1% in water 0.2% in oils and creams	It is used as an antifungal Preservative.
10. Propyl paraben (IP)	----------	It is used as an antifungal

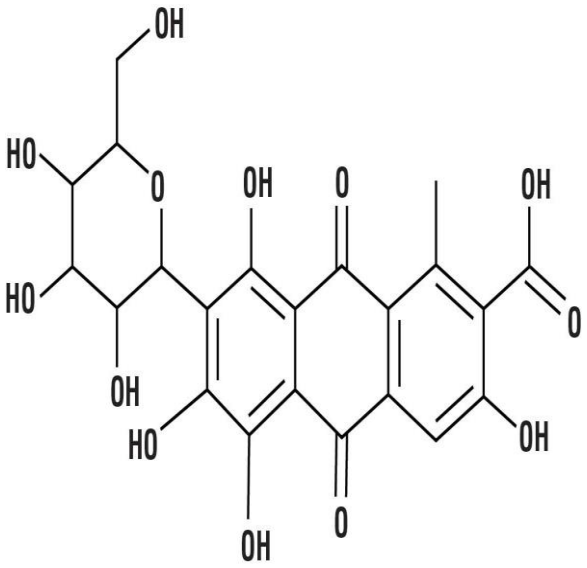
		Preservative.
11. Phenol (IP, USP)	0.5%	It is used as a preservative.
12. Phenyl mercuric nitrate (IP)	0.002%	It finds use as local antibacterial.
13. Sodium benzoate (IP, USP)	0.1%	It is used as an antifungal Preservative.
14. Mixture of methyl and Propyl hydroxy benzoate	0.06% and 0.03%	It is used as an antifungal Preservative.

Coloring agent

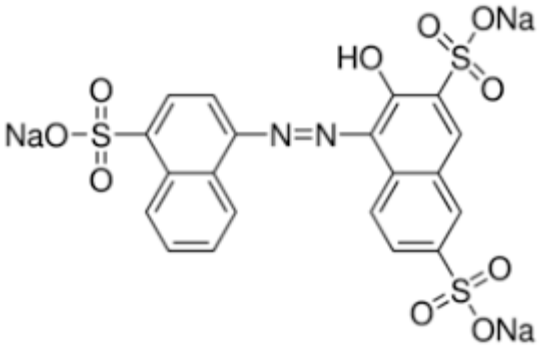
Colorants or coloring agents are used in the processing of food, drugs and cosmetics. A color additive is any dye, pigment or substance which when added to a food, drug or cosmetic or to the human body will impart a color. FDA is responsible for regulating all color additives to ensure that foods containing color additives are safe to eat, contain only approved ingredients and are accurately labeled.

A substance which gives color to pharmaceutical preparations are called coloring agents.

Example: amaranth. Caramel, tartrazine etc.



Caramel



Amaranth dye

Pharmaceutical preparations are colored for following reasons:

1. Increases acceptability

Unattractive medication can be made more acceptable to the patient by the use of color can also be used to make a preparation more uniform when an ingredient in the formulation has itself a variable appearance from batch to batch.

2. For identification

It helps to identify a product in it manufacturing and distribution agents.

The use of different colors for different strengths of the same drug can also help eliminate errors.

3. Stability purpose

Some of the insoluble colors or pigments have the additional benefit when used in tablet coatings or gelatin shells of providing useful opacity, which can contribute to the stability of light-sensitive active materials in the tablet or capsule formulation.

Ideal properties of a colorant

- It should be Non – toxic and have no physiological activity.
- It should free from harmful impurities
- It should be readily soluble in water.
- Its tinctorial (coloring) power should be high so that only small quantities are required.
- It should be unaffected by light, tropical temperatures, hydrolysis, and micro – organism and therefore be stable on storage
- It should be unaffected by oxidizing or reducing agents and pH changes.
- It must compatible with medicaments and not interfere with them.
- It should not have test and odor.

Classification

Coloring agents are classified as follow as

a. Organic dyes and their lakes
b. Inorganic or mineral colors
c. Natural colors or vegetable and animal colors

Organic dyes and their lakes

Dyes are synthetic chemical compounds that exhibit their coloring power or tinctorial strength when dissolved in a solvent.

Example: tartrazine (lemon yellow)

Sunset yellow

Erythrosine

Lakes have been defined by the FDA as the Aluminum salt of FD&C water soluble dyes.

Inorganic or mineral colors

Stability towards light is an important characteristic displayed by this materials, some of which have a useful opacifying .capacity, e.g. titanium dioxide, ferric oxides etc.

Natural colors or vegetable and animal colors

This is a chemically and physically diverse group of materials.

Some of these colors are the products of chemical synthesis rather than extraction from natural source.

E.g. ß carotene

Flavoring agents

Flavoring agents are added to increase patient acceptance. The four basic sensations are salty, sweet, bitter, and sour. It has been proposed that certain flavours should be used to mask these specific taste sensations.

Example:

Clove oil, citric and syrup, glycerin, rose oil, orange oil, menthol etc.

Flavouring agents are incorporated into a formulation to give the tablet a more pleasant taste or to mask an unpleasant one. The latter can achieved also by containing the tablet or the drug particles.

Flavouring agents are often thermolabile and so cannot be added prior to an operation involving heat. They are often mixed with the granules as an alcohol solution.

Flavours added to solutions can make a medicine more acceptable to take especially if the drug as an unpleasant taste.

Flavours should be choosen to mask particular taste types, e.g. fruit flavor helps to disguise an acid taste.

The age of the patient should be taken into account when selecting a flavor, as children will tend to enjoy fruit or sweet flavours.

The flavor and color should also complement each other.

Different types of flavors

a. Natural flavor: essential oil, oleoresin, essence or extractive, protein hydrolysate which contains the flavoring constituents derived from a spice, fruit, vegetables, edible yeast, herb, bark, bud, root, leaf or similar plant material, meat, seafood, eggs, dairy products etc.
b. Artificial flavor: Any substance used to impart flavor that is not derived from a spice, fruit, vegetables or anything mentioned above
c. Spice: Any aromatic vegetables substance in whole, broken, or ground form, except substance traditionally regarded as foods, such as onions, garlic.

Sweetening agents

Sweetening agents are substances that sweeten and mask the taste of food, beverages and medications to make them palatable to the consumer. The sweetening agents are sugar, saccharine or other low-calorie synthetic products.

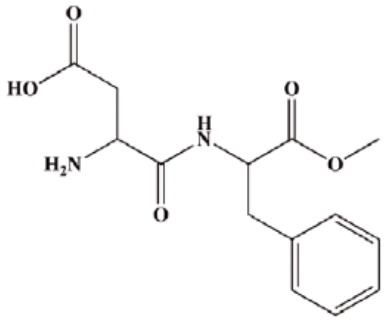
- Sweetening agents are the substances which are added to a drug formulation to mask its bitter taste.
- Sugar is the most widely used natural sweetening agents.
- It imparts viscosity to drug and also even act as preservatives for liquid dosages form.
- Sugar has lot of disadvantages like dental caries, high blood sugar, calories etc.
- Among this three are various substitutes available over sugar.

These are 2 types of substitute which are used as sweeteners,

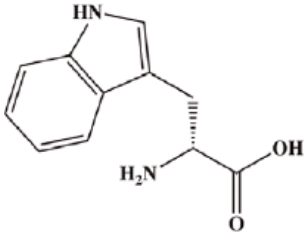
- Natural sweeteners e.g. honey, steiva, maple syrup etc.
- Artificial sweeteners e.g. Saccharin, aspartame etc.

The intensity and duration of the aversive attribute of the drug active (bitter, salty, or source) informs identification of candidate sweeteners. For example many drug actives have a long –lived bitterness profile that for palatability requires the lingering sweeteners afforded by many artificial sweeteners.

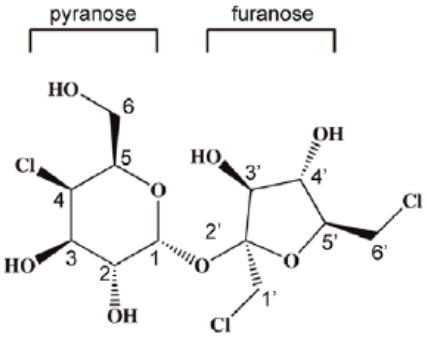
The artificial sweeteners typically exhibit good solid state stability across the board, but some have poor stability in solution. For example, aspartame readily hydrolyzes in aqueous environments, and a liquid aspartame sweetened product would experience drastic changes by 6 months storage.



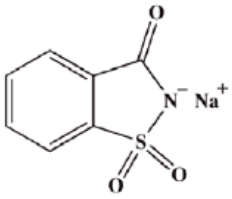
aspartame



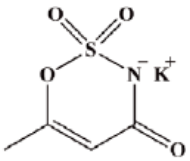
D-tryptophan



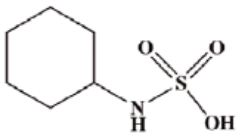
sucralose



saccharin Na



acesulfame K



cyclamate

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