Subject Code: US06CCHE24
Applied Chemistry
Semester: VI
UNIT : II : Drugs

By Dr. B. C. Dixit

Introduction, Classification of drugs. Introduction and classification of following selected class of drugs. Hypnotics, sedative and anticonvulsants, Histamine and antihistaminic agents, Hematological agents, Antipyretic and analgesics, Mode of action of antipyretic drug. Anthelmintics, Antimalerial, Antiseptic, Sulphanilamides, Mechanism of action of sulpha drug. Antitubercular and antileprosy drugs. Synthesis and uses of following drugs : (i) Nirvanol (ii) Phenobarbitone (iii) Dimenhydrinate (iv) Novalgin (v) Phenylbutazone (vi) Hetrazan (vii) Atenelol(viii) Chloroquine (ix) Lidocaine, (x) Sulphamethazine, (xi) Sulphafurazole (xii) PAS (xiii) Acedapsone (xiv) Tolbutamide .

Que. Discuss the terms? (Define).

Drug: "It is a substance or a compound which is used to prevent or cure the disease in man or other animals."

Que. What are the requirements of an ideal drug?

(i) When it is administrated to the host, its action should be localized at the site where it is desired to act.
(ii) It should act in a system with good efficiency and safety.
(iii) It should not have any toxicity.
(iv) It should have minimum side effects.
(v) It should not injure host tissues or physiological process.
(vi) The host cell should not acquire resistance to the drug after some time.

Definitions :

(i). Medicinal Chemistry: It is field of science which applied the principles of chemistry and biology to the creation knowledge of therapeutic action.

(ii). Pharmacy: It is concerned with the collection, preparation and standardization of drugs. (i) It includes the cultivation of plants which serve as drugs. (ii) The synthesis of chemical compounds. (iii) The chemical analysis and testing of the agents used for medicinal purposes.

(iii). Pharmacology: It is a branch of science which deals with the detailed study of drugs in terms of beneficial and harmful action on living animals and organs. The part of medical science which cover and study of medicines and drugs, including their action, their use and their effect on the body.

(iv). Pharmacophore: The physicological activity of the drugs depend upon the presence of particular functional groups or structural units. Such a parts of the drug which causes the actual physicological effect is known as pharmacophore.

(v) Pharmacodynamic Agent: The drugs which stimulate or depress various functions of the body so as to provide relief from symptoms of discomfort are known as Pharmacodynamic Agent.

(vi). Metabolites: The substance which takes part in metabolic reaction known as metabolites. E.g. p – Amino benzoic acid (PABA).

(vii) Anti – Metabolites: A chemical substance which block metabolism is known as Anti–Metabolites i.e. Sulphonamide.
(viii) Bacteria: These are group of microorganisms which are classified in to mainly two classes (i) Gram +ve & (ii) Gram –ve, depending upon their staining characteristics. Bacteria which retain violet stain of Gram's reagent (crystal violet +iodine) are known as gram +ve bacteria on the other hand bacteria which do not retain the violet stain of gram's reagent are known as gram –ve bacteria.
(ix) Virus: These are very small microorganisms which are parasitic within living cells. These differ from bacteria in having only one kind of nucleic acid, either DNA or RNA.
(x) Fungi: It is a low form of vegetable life including many microscopic organisms. It does not contain chlorophyll & generally grow on organic matter like leather, state food, sugar, fruit etc. It causes superficial and systemic disease in living beings.
(xi) Mutation: The sudden alteration of a gene is known as mutation. This may be spontaneous or induced and is inherited by subsequent generation and retain until further mutation. Spontaneous mutation takes place without ape sent influence from out side the cell while mutation is produced by known agent out side the cell e.g. u.v. rays, x-rays.
(xii) Vitamins: These are organic compounds which are required by the animals for maintenance and normal growth of the life. These are supplied by food because these cannot be synthesized by animals, except vitamin. They are divided into two classes.
i) Water Soluble: Vitamins of Group B & C.
ii) Fat Soluble: Vitamins A, D, E and K.

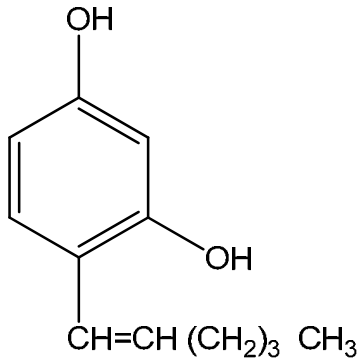
Classification of Drugs:
Que. What are drug? Classified them on the bases of their therapeutic actions or chemo therapeutic actions.
Ans. Drug may be classified in the following ways.
(I) On the bases of their therapeutic action.
(II) On the bases of their chemical structure.
(I) On the bases of their Therapeutic action:
According to the therapeutic actions the drugs are classified into two broad types.
(A) Psychopharmaco dynamic agents or CNS agents:
These are the drugs which actions the various functions of body. These drugs are further classified as followed.
(i) Non-selective CNS depressants e.g. alcohol and trichloroalcohol.
It is drugs use to make person or animal calmer.
(ii) Selective modifiers of CNS: Tranquilizers.
They are effective in reducing excitation and aggressiveness in case of mental disorder. E.g. alkaloids and indole derivatives.
(iii) CNS Stimulate: A substance which make the mind or body more active. Antidepressants, or metrazole.

(iv) Blocking agent (Adrenergic stimulate): The blocking agent can be divided in to two groups and act directly on the cell to increase excitation or to decrease inhibition in the tissues activities.
(a) Compounds with –OH group substituted in the -3 & -4 position of aniline ring are called catechol amines.
(b) Those which do not contain –OH group are known as Non- catachol amines.

(v) Drugs acting on Cardiovascular hemotopoietic and renal system
(vi) Pharmacodynamic agents
(vii) Metabolic disease and endocrime functions

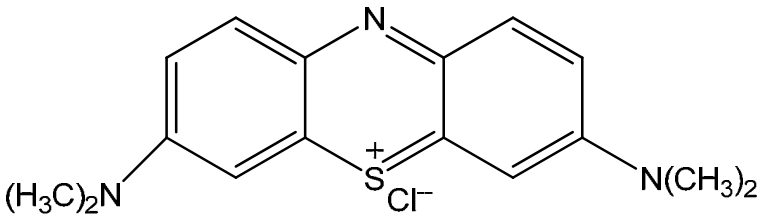
B) Chemotherapeutic agents:

Chemotherapy is the use of chemical agent in the treatment of infectious disease. The chemical agents used are known as chemotherapeutic agents. The agents are designed to kill the invading organisms without harmful effect on host. They may be further divided into following class;
i) Organometallic Compound.
ii) Anthelmintic Agents.
iii) Antimalarial.
iv) Anti Protozoals.
v) Anti Septic.
vi) Anti Fungal.
vii) Anti Bacterial.
viii) Anti Biotic.
ix) Anti Tubercular and Antileprosy drug.
x) Anti Neoplastic drug.
(i) Anthelmintics: These are the drugs which are used to kill or remove the parasitic worms such as hook worms, round worms, tape worms etc.
Those anthelmintics, which kills the worms are called vermicidal, while those which helps in expelling them by making the environment uncomfortable for living them are called vermifuge.
Caprokol : It is well known urinary tract antiseptic. It is also used for the treatment of tape worm infections.

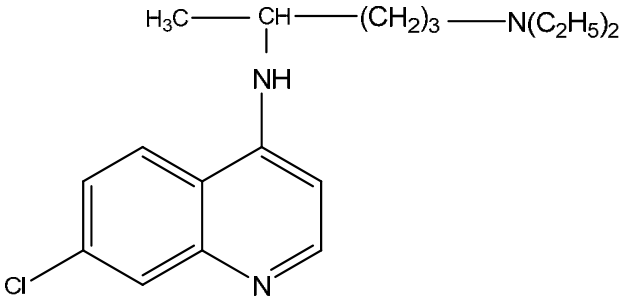


(ii) Antifungals: The drug which are use against fungus infections are known as antifungal agent. They have been divided in to tow groups.

i) Those which are use local infections.
ii) Those which are use for systematic infection. e.g. salicylic acid, benzoic acid.
(iii) Antibiotics: It is chemical substance produce by or derived from living cells. They can capable in small concentration for inhibiting the life process of micro – organism. E.g. peneciline, steptomycine.
(iv) Antiseptic: Antiseptic is a substance which prevent the growth of micro – organism as long as it remain in contact with them. E.g. phenylsalicylate, vioform. These type of drugs are applied locally [directly to the skin/wound] are known as antiseptic drugs. Generally the term antiseptic includes those anti-infective agents, which are applied to living tissues. Thus antiseptics are bacteriostatic and do not necessarily sterilize the surface under treatment.
CIDEX : It is used as a sterilizing solutions for equipments and instruments [surgical instruments, which can not be heated for sterilization]
METHYLENE BLUE : it is mainly used as an intestinal and urinary antiseptic.



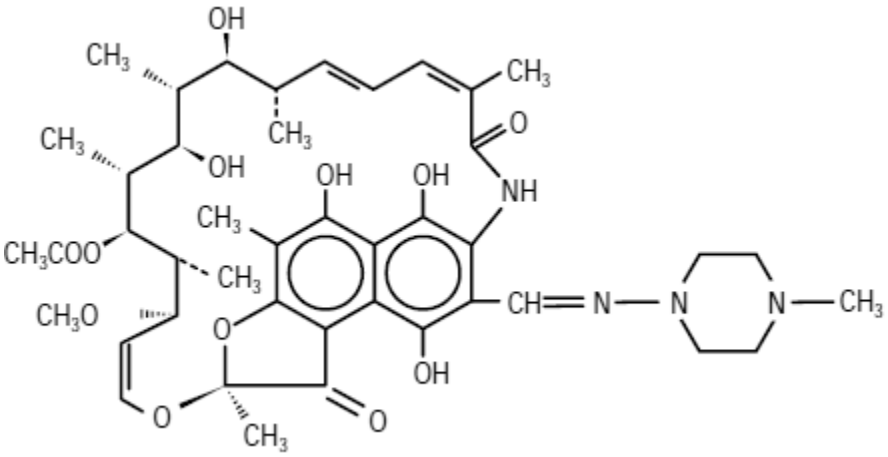
v) Antimalarial : These are the substance capable of killing sporozoa of genes plasmodium like plasmodium vivax, plasmodium-malaria and plasmodium-falciparum.
Chloroquine :



Its hydrochloride is used for injections, where as its sulphates and phosphates are used as tablets.
(vi) Antitubercular and antileprosy drugs:
Antitubercular drugs:
Drugs used to cure tuberculosis in human are known as antitubercular agents. Tuberculosis is a system infections disease, caused in man by Mycobacterium tuberculosis and Mycobacterium bones organism. The different chemotherapeutic agents are:
p-aminosalicylic acid, isoniazide, viomycin, ethambutol

Rifampin : It is semisynthetic antibiotic, obtained from rifamycins which represent a group of chemically obtained from streptomyces mediterrani. It has found to be

highly effective against Mycobacterium tuberculosis and have drug resistant infection. It has no side effect.



Antileprosy drugs :

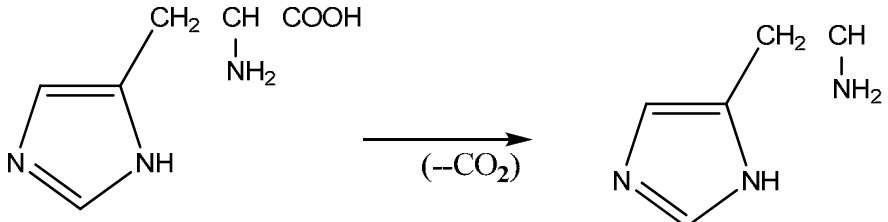
These drugs are used to cure leprosy are known as antileprotic drugs. Leprosy is a slow endemic disease by Mycobacterium leprate.

Various antileprotic drugs are :

Dapsone, Acedapsone, solapsone, promizole

(vii) Histamine and anti histamine agents:

Histamine agents: Histamine is found in all the organs and tissues of human body and is found in very small amounts. It is produced by decarboxylation of Histidine.



HISTIDINE HISTAMINE

Functions of Histamine agents :

(i) It decreases blood pressure by dilating the capillaries and increase the heart rate.

(ii) It play and important role in human allergy.

(iii) It is important for the rapid growth of tissues, particularly after wounds.

(iv) In the lungs it act on muscles and producing Broncho-constriction constriction.

(v) In the gastro intestinal tract, histamine has a stimulating action on certain excretory glands, causing an increasing in the secretion of the acid in the stomach, which may cause gastric and ulcer problems.

Anti-histamine agents:

The effect of histamine can be overcome using anti histamine agents.

Chemically histamine is inactivated by using certain compounds like Formaldehyde Carbondioxide, enzyme histamine. This compounds combines with histamine.

Antihistamine agents initiating certain pharmacological response in the body, which oppose the action of histamine.

"It is a drug which is capable of diminishing or preventing several pharmacological effects of histamine".

Uses :

Antihistamine agents are quite beneficial in several fever.

This are also used to relieve serum sickness, urticaria, motion sickness, and nausea of pregnancy.

Antihistamine agents along with analgesic agents are widely used in the treatment of common cold.

Side effects of Antihistamine agents:

It depress CNS and cause sedation leading leading to drowsiness, dizziness and dryness of mouth, nose and throat.

Benadryl :

$$(CH_3)_2NCH_2CH_2OCH(C_6H_5)_2$$

It is used in the treatment of various allergic conditions. It is used in the treatment of hey fever, bronchist, and asthama. It is used in some cough mixture.

Avil :

$(CH_3)_2NCH_2CH_2CH(C_6H_5)_2$

It is most powerful antihistamine drug and is very persistent in his action.

(viII) Anaesthetic: Anaesthetic are the chemical which produce insensibility to the vital function of all types of cells. Especially those related with CNS. It produce temporary insensibility to pain or feelings in the body or particular organ. Which has under go operation. That is it causes the loss of sensation to pain. They are classified into two types.

a) Local Anaesthetic: They do not affect the whole body but make only a part of the body insensitive to pain or feelings. e.g. cocaine, procaine etc.

b) General Anaesthetic: There are the substance use to make whole body insensitive to pain or feelings. e.g. Chloroform.

vii) Cardiovascular agents: They have direct action on the heart other part of the vascular system and they are the distribution of blood supply.

viii) Diuretics: They increase the output of urine by the kidneys. They are used for the excretion of sodium and chloride. They employed for the treatment of edema, i.e. congestive heart failure edema of pregnancy e.g. caffeine, theophylline etc.

ix) Hematological agents: These are the drugs which act on the blood and blood forming organs. These are of two types :

(i) Coagulant and anticoagulant agents

(ii) Antianemic agents. (Heparine and Worfarin).

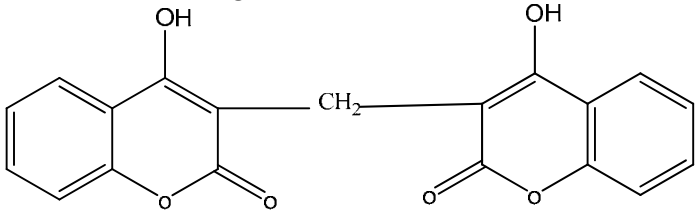
(i) Coagulant agents :

These are the drugs which stops the excessive bleeding by clotting of blood. [Haemophilia]
In normal conditions the coagulation of blood in the vascular system is prevented by an organic substance called heparin, which is produced by liver.
If blood injury occurs, the blood should coagulate in normal condition but in abnormal conditions the blood does not coagulate and excessive bleeding occurs. e.g. Vitamin K1, K2, proteins and amino acid, oxidized cellulose, carbazochrome salicylate.

Anti-coagulant agents :

The substance which retards clotting of blood are called anticoagulant agents.
Requirement of an ideal anticoagulant agents:
It must be useful orally. It must be produce rapidly on onset of its action.
It must be cheap. Its side effect should be minimum. There must not be any cumulative action of toxicity.

Dicoumarol or Dicuman : It is used alone or together with heparin in the treatment of Intravascular clotting.



(ii) Antianemic agents : In case of disease the balance between number of red cells and percentage of haemoglobin upset. As a result there is deficiency in the oxygen carrying capacity of blood is known as Anemia. Most of anemia caused by deficiency of concentration of Iron, Vitamin B12 or Folic acid.

x) Antipyretic and Analgesic drugs:

Antipyretic drugs : An antipyretic drug is responsible for lowering the temperature of feverish organism to normal but has no effect on normal body temperature states.

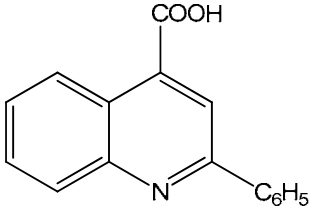
Mode of action of Antipyretic drugs :

Hypothalamus plays an important role in maintaining the balance between heat production and heat loss. Therefore, hypothalamus is known as thermostat of the body. In case of fever, there exist the balance between heat production and heat loss but the thermostat is only set at higher level. Under such conditions, the antipyretic drug helps to reset the thermostat for normal temperature. Here heat production is not inhibited but heat loss is increased by increasing peripheral blood flow, which thus increases the rate of perspiration. This causes the body to loss heat and subsequently lowers the body temperature.

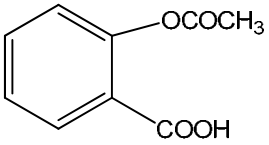
x) Analgesic drugs:

Analgesic is a drug, which relieves the pain without loss of consciousness by a consequence of febrifuge effects. The action of an analgesic on the CNS to decrease the sensation of pain.
These are classified as :
(a) Narcotics :

They produce analgesic and sleep, also in high doses causes unconsciousness.
Alkaloid : Chinchophen : It is used in the treatment of Gout.

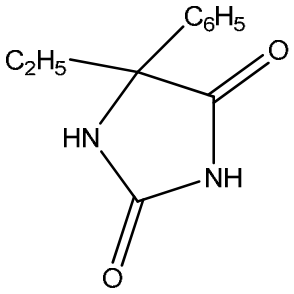


(b) Non-narcotics :
These are not so potent and do not causes addiction.
Aspirin : It is used as antipyretic, analgesic and antirheumatic agents.

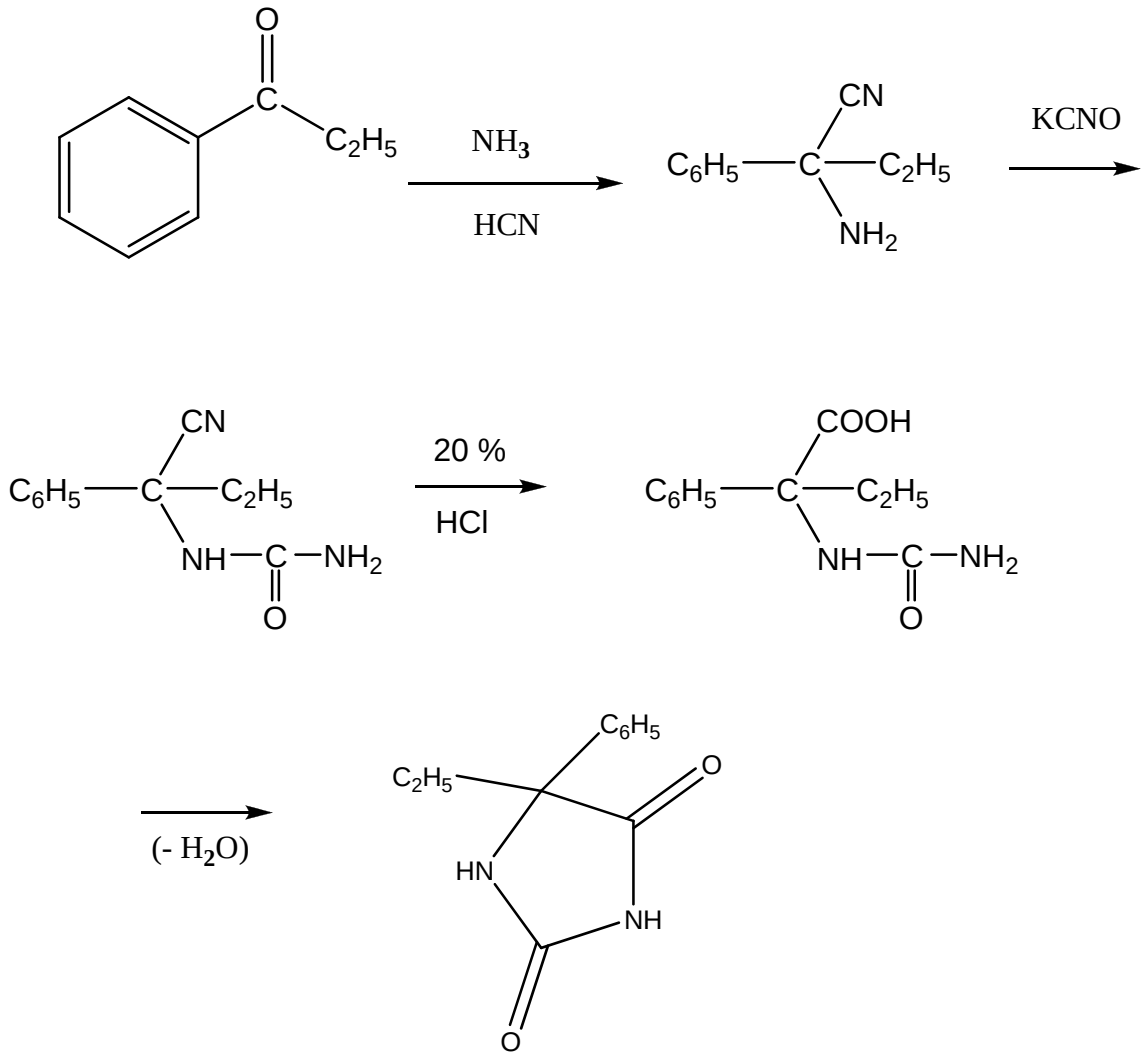


Que. Discuss the terms OR Explain the following terms.
1) Sedative. 2) Anaesthetic. 3) Hypnotics. 4) Cardiovascular agent. 5) Virus. 6) Gramative and Gramative bacteria. 7) Antifungal. 8) Antibodies. 9) Pharmacy. 10) Antimetabolites. 11) Diuretics. 12) Anthelmintics. 13) Hematological agents. 14) Bacteria. 15) Vitamins. 16) Hormones.
(i) Sedatives: Sedatives are central nervous system depressants that reduce restlessness and emotional tension without producing sleep. i.e. metharbital, ethinamate.
(ii) Hypnotics: Hypnotics are central nervous system depressants that produce sleep to reduce restlessness and emotional tension. i.e. trichloro ethanol, chloral.
(iii) Anesthetics: Those drug which produce insensibility to the vital functions of all types of cells, especially those of the nervous systems. It produces temporary insensibility to pain or feeling in the whole body or a particular organ which has to undergo operation. They may be classified into two groups.
i) General Anesthetics – Chloroform.
ii) Local Anesthetics – Cocaine, Benzocaine.

1. NIRVANOL :



Synthesis:



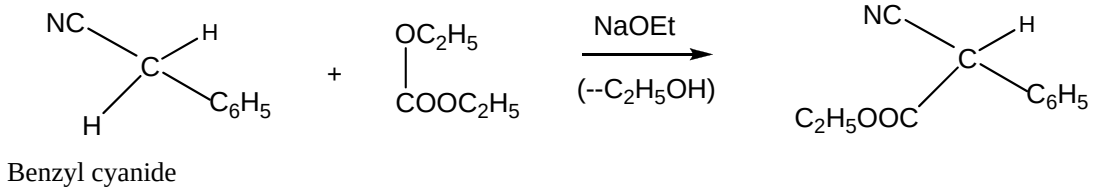
USES :

It is used in the treatment of cholera.

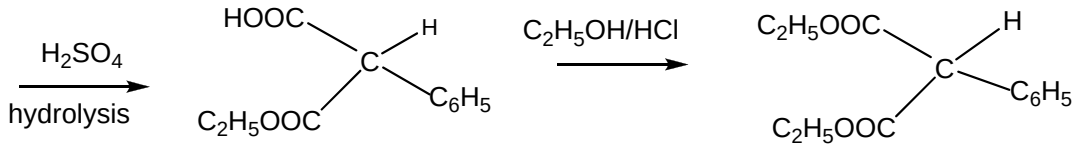
Due to its high toxicity it was replaced by other hypnotics.

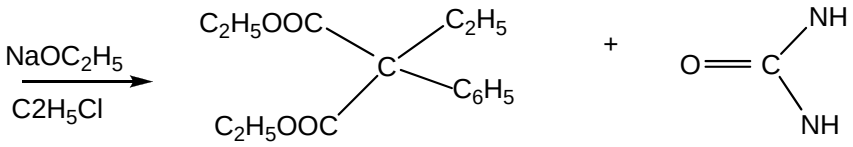
It is HYDANTOIN derivatives of most potent anticonvulsant class of drug.

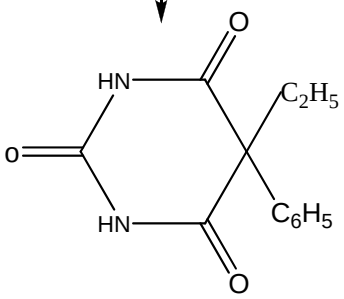
(ii) Phenobarbitone



Benzyl cyanide

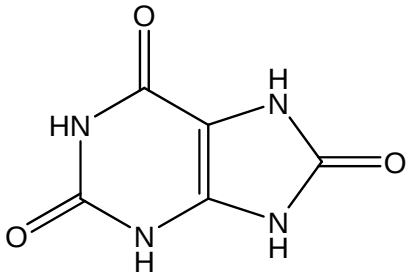




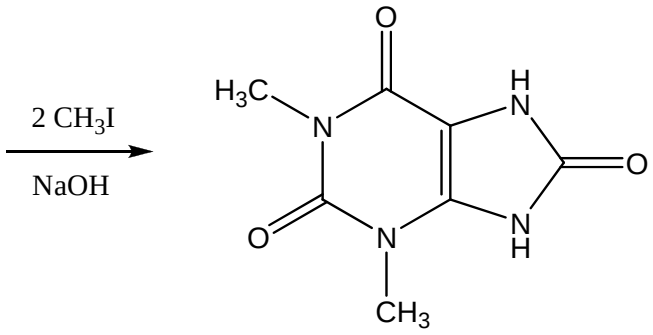


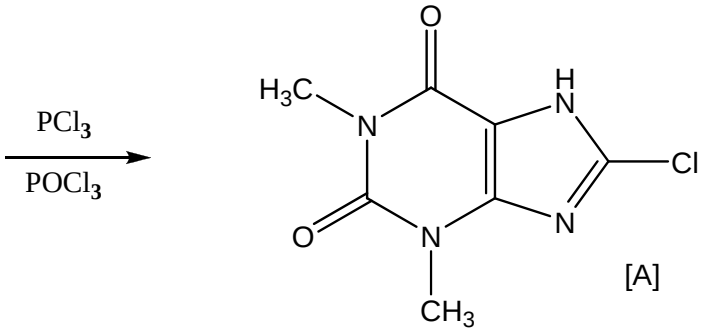
USES : It is used as a sedative and hypnotics. It is slower in its action but its duration is 10-16 hours. It is also effective in the control of epileptic seizures. It can be safely given for the treatment of general convulsion in children.

(iii) Dimenhydrinate

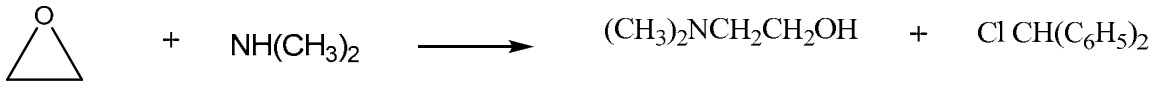


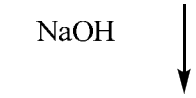
Uric acid





[A]

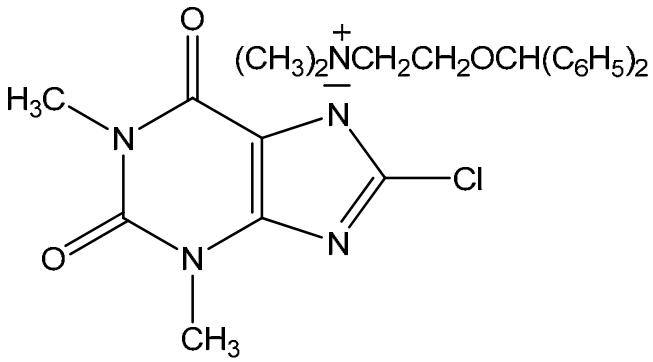




$(CH_3)_2NCH_2CH_2OCH(C_6H_5)_2$

[B]

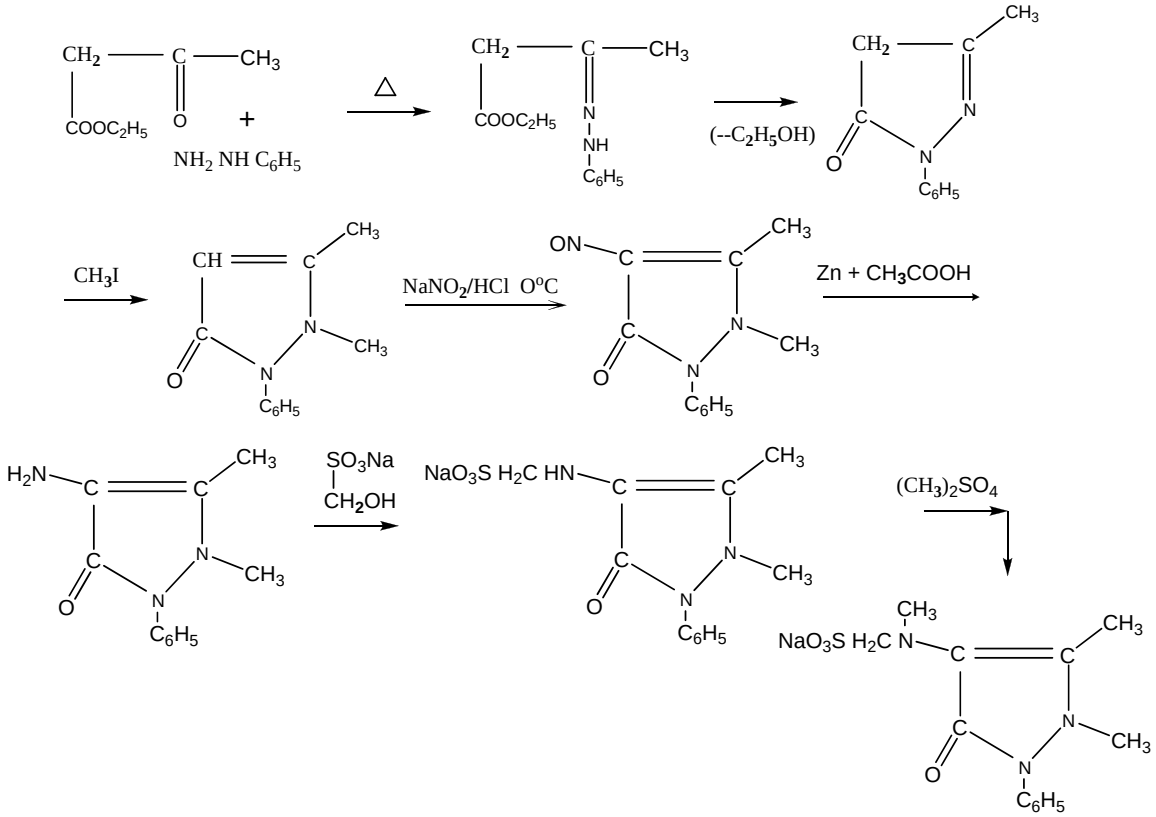
A + B



USES : To overcome the side effect of Benadryl, the quaternary salt of Benadryl with 8-chlorotheophylline is used.

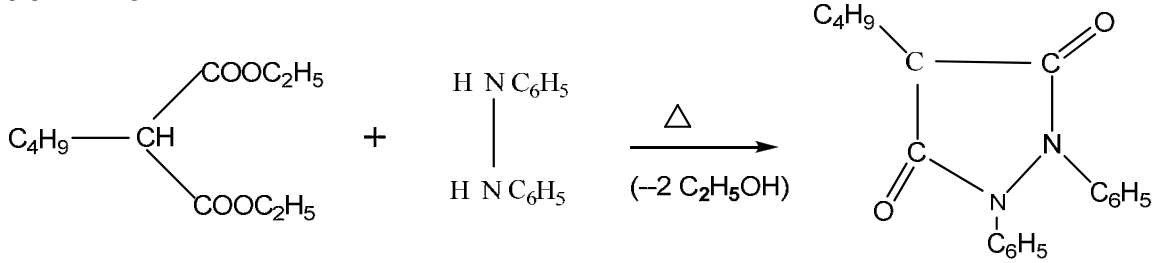
It is used for the control of motion sickness and sickness of pregnancy.

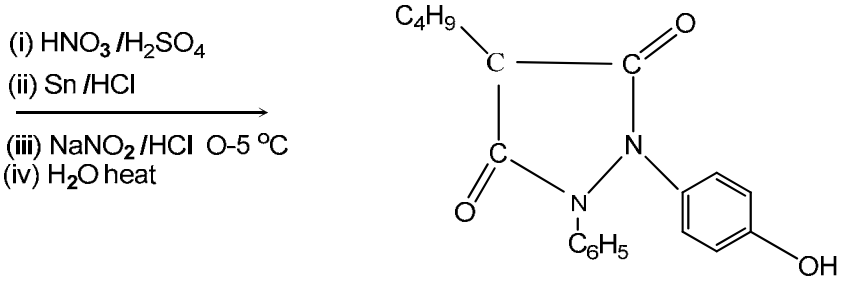
(iv) Novalgin



USES : It is an antipyretic and analgesic drugs. It lowers the body temperature in case of fever. It also subside headache and body pain.

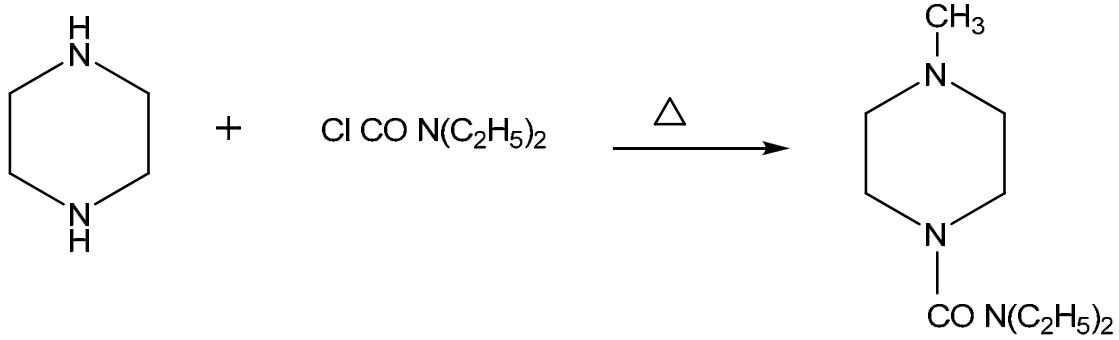
(v) Phenylbutazone





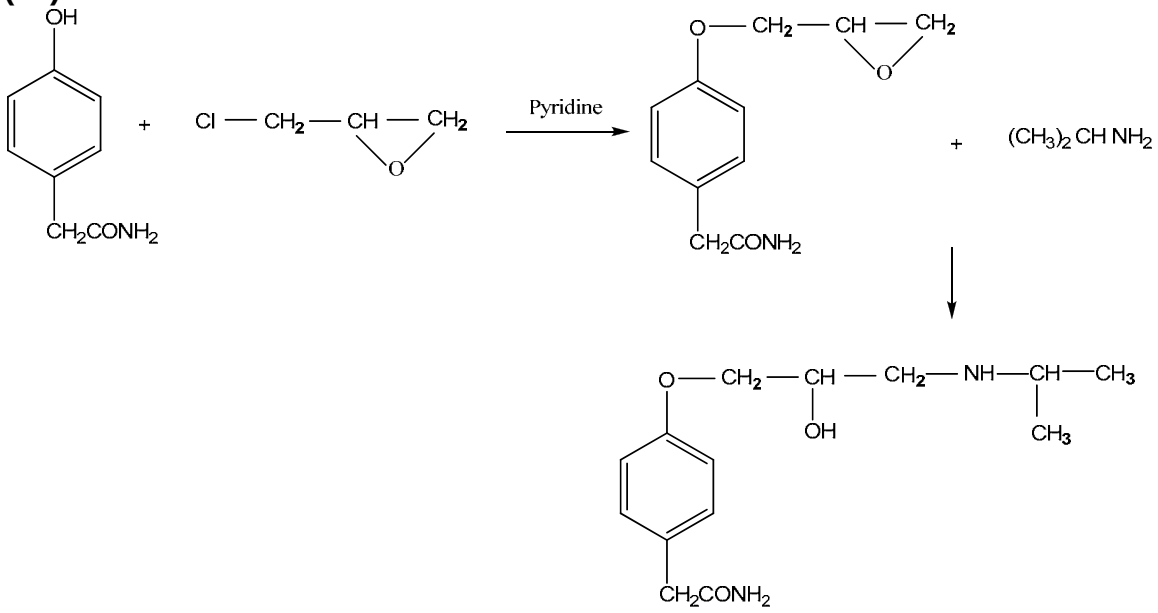
USES : It is used in the treatment of arthritics and certain allied conditions. It appears to be most useful in spondylities. Its oxide derivatives is more potent and have less toxic side effects.

(vi) Hetrazan



USES : It is used as anthelmintics to remove worms in children.

(vii) Atenelol

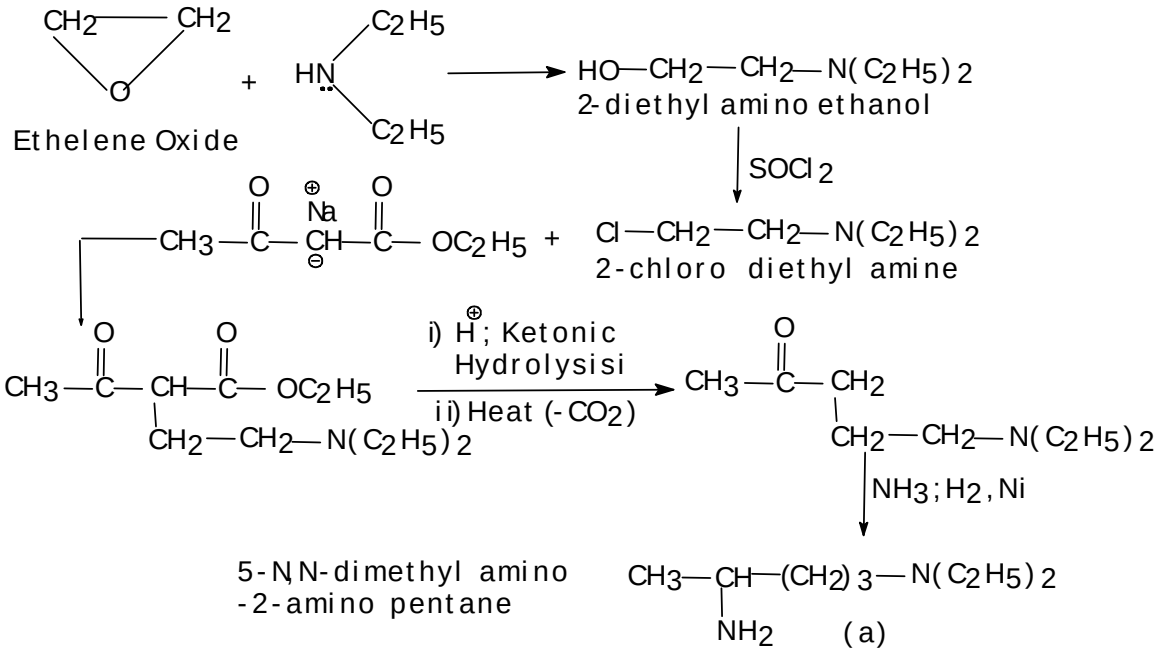


USES : It is a Beta-blockers. It is used for antihypertensive, antianginal, antiarrhythmic agents etc.

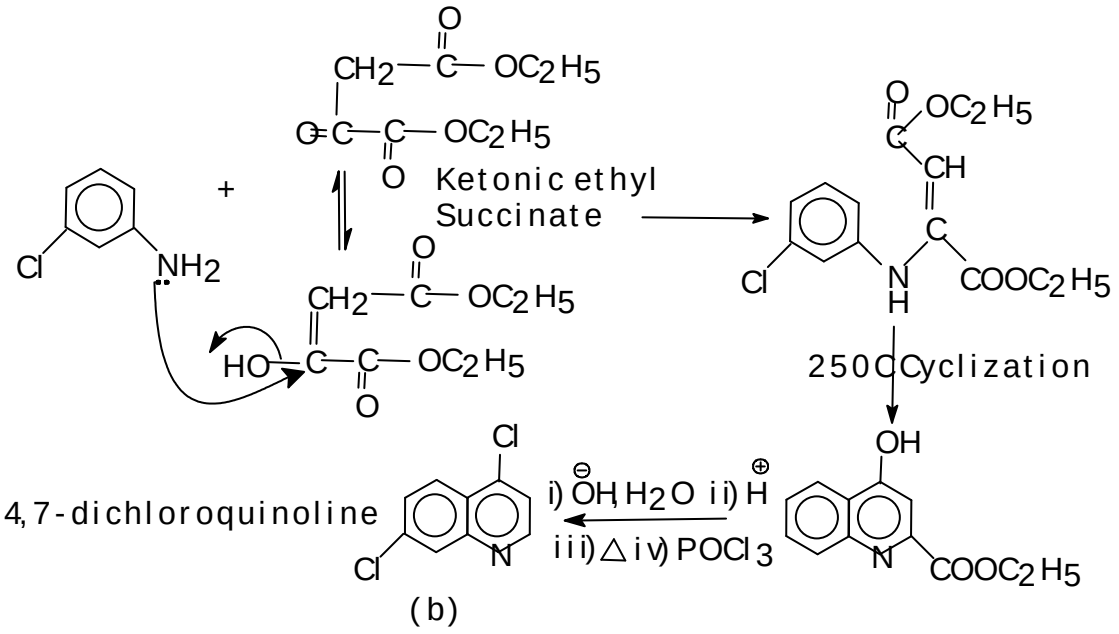
(viii) Chloroquine

5.) CHLOROQUINE: It's synthesis involves following three steps;

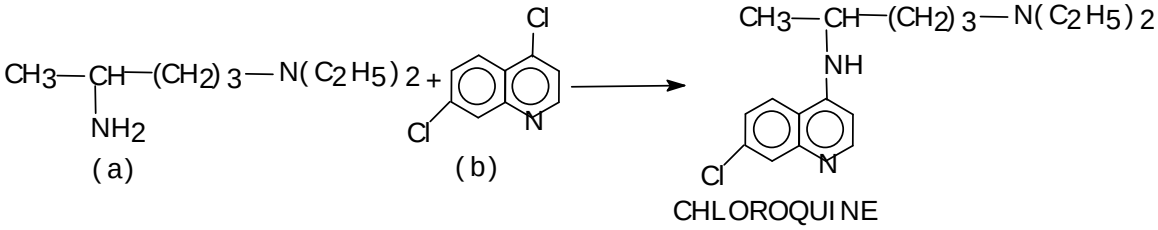
a) Synthesis of side chain.



b) Synthesisof4,7-dichloroquinoline.

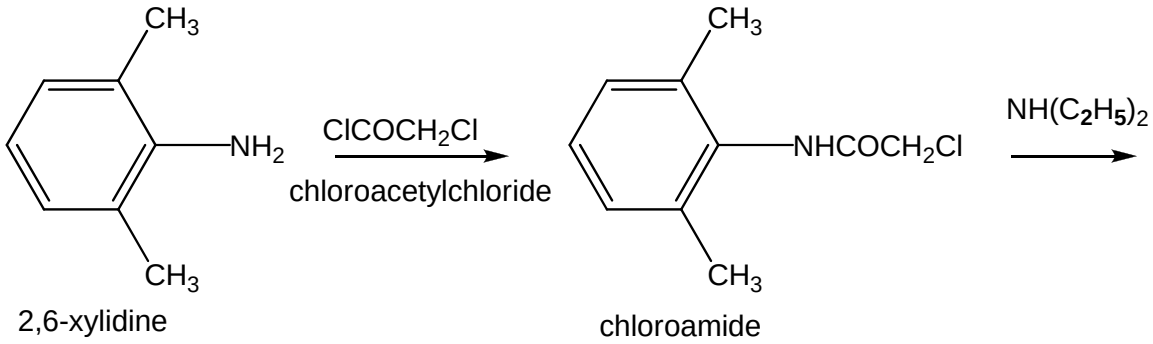


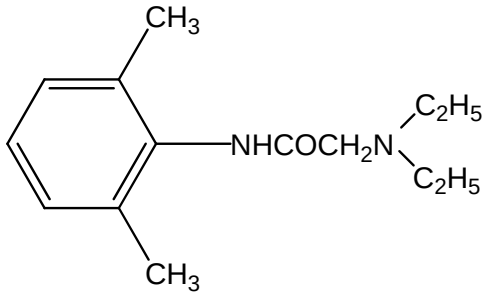
c) Condensation of (a) & (b).



Application: (i) It's hydrochloride is used for injections. Where as it's Sulphates and Phosphates are used as tablets.
(ii) It is found active against P – vivax and P – falciparium malaria.
(P = Plasmodium).
(iii) It cause side effects of general weakness, uneasiness, vomiting, diarrhea etc. but as soon as use of drug is stopped side effect tends to disappear.

(ix) Lidocaine (xylocaine) :



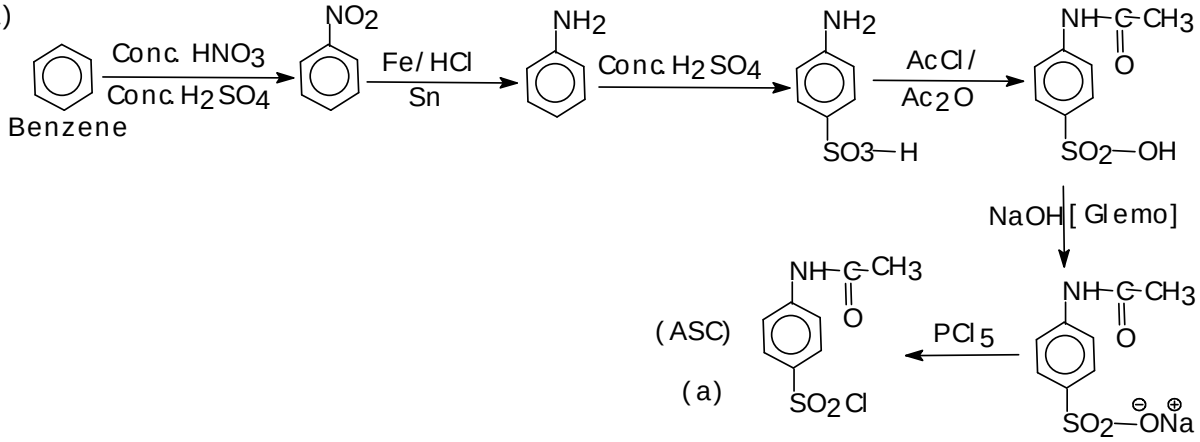


USES : It is used as antiarrhythmic drugs. It is also used in dental surgery, wounds and hemorrhoids.

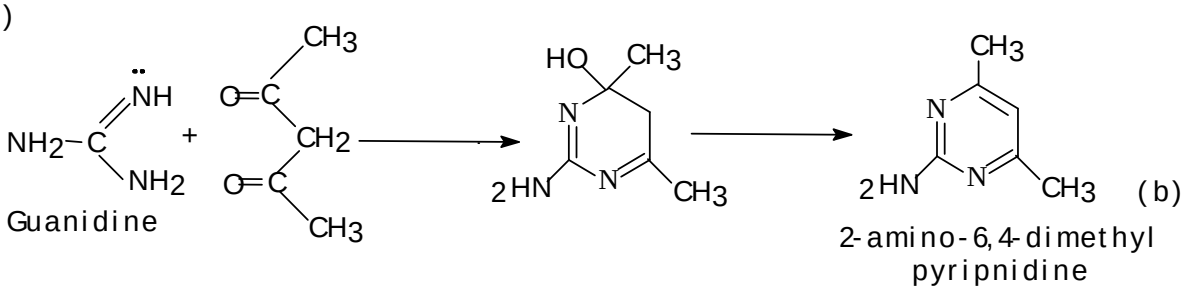
(x) Sulphamethazine,

11.) SULPHAMETHAZINE (SULPHAMEZATHINE):

(a)

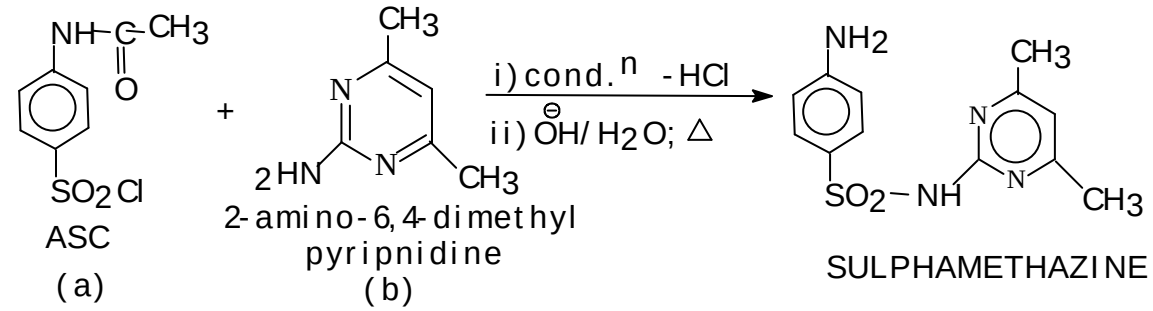


(b)



2-amino-6,4-dimethyl pyripnidine

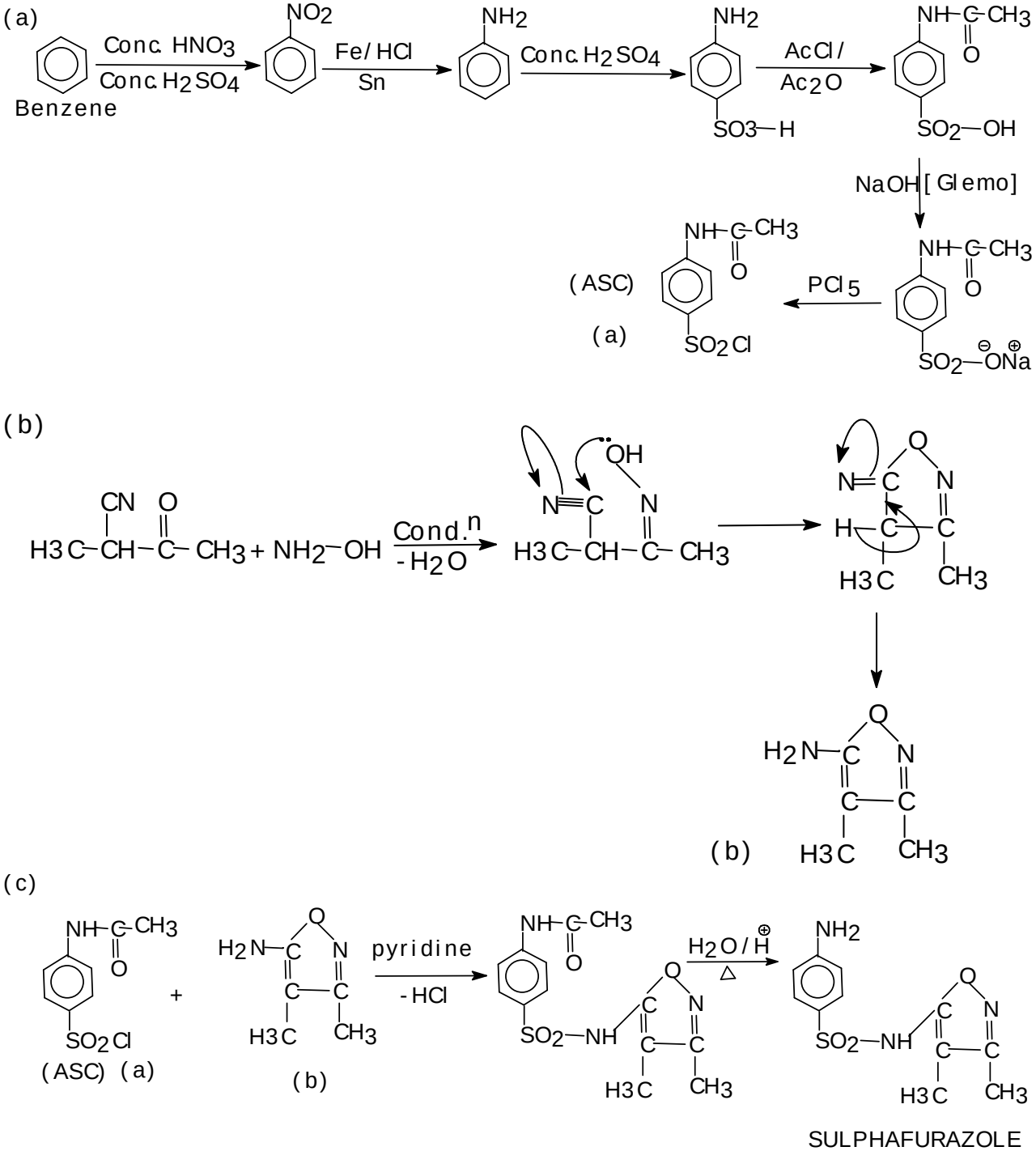
(c)



Application: (i) It is used as less potent than sulphadiazine.
(ii) It is absorb more rapidly but excreated more slowly. As it is soluble in uric acid, The possibility of kidney damage from the use of drug decreases.

(xi) Sulphafurazole

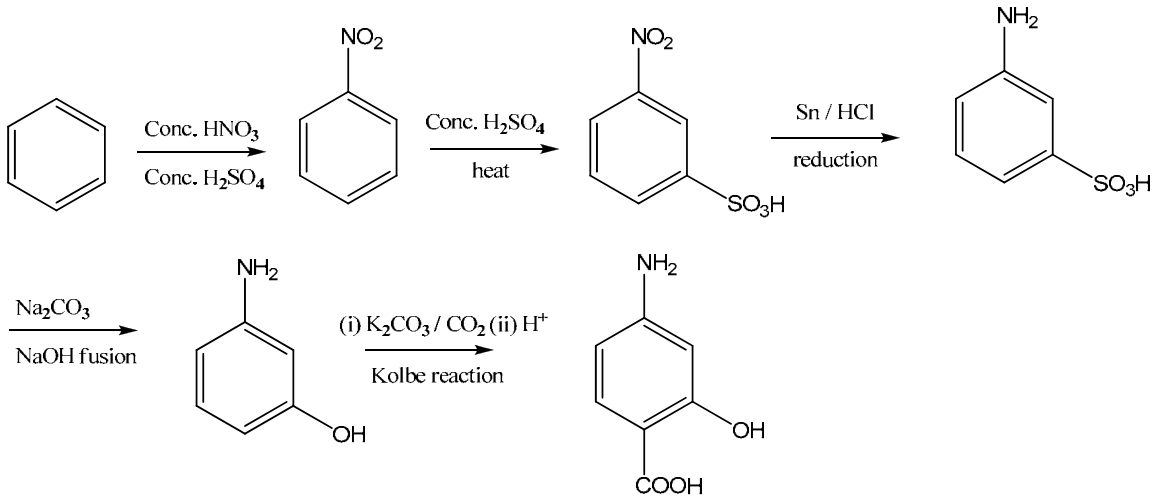
12.) SULPHAFURAZOLE (SULPHISOXAZOLE):



SULPHAFURAZOLE

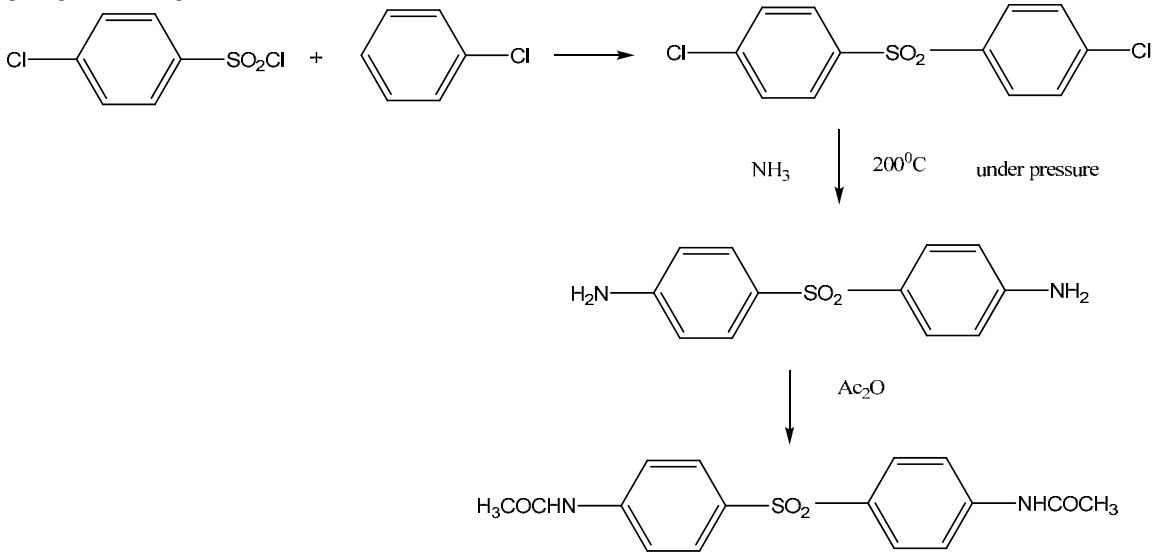
Application: It is soluble over a wide range of pH. It is for infection involving those bacteria which are sensitive are sulpha drugs. It is found effective in the treatment of gram negative bacteria various infection. It's acetyl derivative. It's substance orally administration (tablet) or liquid of drug (syrup).

(xii) pare-Aminosalicylic acid [PAS]



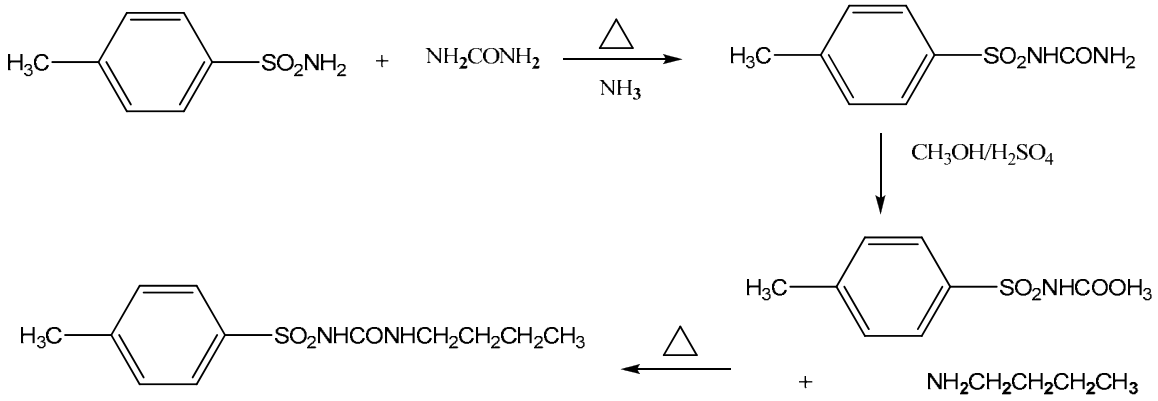
USES :

(xiii) Acedapsone:



USES : It is an anti T B agents.

(xiv) Tolbutamide .



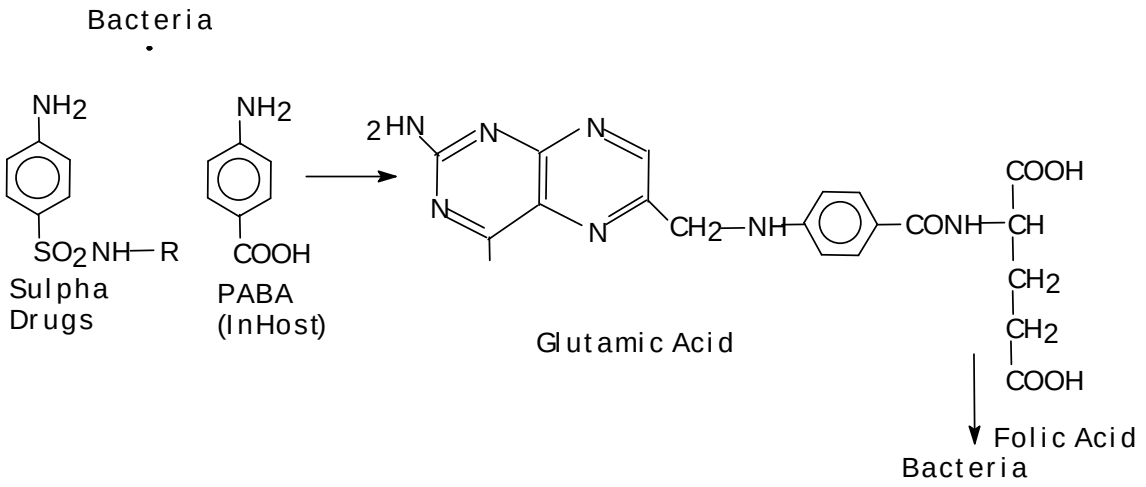
Uses : It is an oral hypoglycemic agent. It is safe drug for elderly patients.

Mechanism of Sulpha Drugs:

Sulpha Drugs are bacteriostatic but not bactericide. i.e. sulpha drugs do not kill the bacteria directly but they prevent the growth and multiplication of bacteria. The bacteriostatic properties of sulpha drug (sulphonamide) is found due to their similarity in structure with that of

p – amino benzoic acid (PABA). The PABA is an important component for the normal functioning of the vital processes in bacteria. This PABA is required for the synthesis of folic acid, which is essential for the growth and multiplication of Micro – Organism.

Thus in Micro – Organism (bacteria), due to similarity in structure with that of PABA; the sulphonamides compete with (it) PABA, for the attachment to the enzyme which converts PABA in to folic acid. Thus in presence of sulpha drugs enzyme is thus blocked and the synthesis of folic acid stops in Micro – Organism. There fore due to the lack of folic acid; the Organism gets weakened and they become unable to grow and multiply; and hence the White Blood Cells (WBC) and reticnloendothelial system of the host kills the bacteria and eliminate the infection in host.



-Differentiate between Bacteria and Virus.

Viruses consist of a piece of genetic material, such as DNA or RNA (but not both) surrounded by a protein shell called a capsid. They are 10 to 100 times smaller than the smallest bacteria. They are not considered living organisms.

Bacteria are simple, single celled organisms, called prokaryotes, which means their DNA is contained within a certain area of the cell called the nucleotide, but not enclosed. Bacteria are living things.

REFERENCE BOOK :

1. Synthetic Drugs 6th Ed. by Gurdeep R. Chatwal.
2. Medicinal chemistry 3rd Ed. by Ashutosh Kar.