

## Sedatives and Hypnotics

Hypnotic drugs produces sleep resembling natural sleep. Whereas Sedatives are the drugs which reduce excitement. Both the drugs are central nervous system depressant and this difference is merely quantitative.

Sedative and hypnotics when given in large doses may produce anaesthesia poisoning which may be fatal in some cases.

An ideal hypnotic agent should have the following properties:-

They should be effective when administered orally.

These drugs should not produce addiction, tolerance or habituation.

It should be non-toxic, non-irritant and should not produce hang-overs.

It should be cost effective

An overdose should not be very harmful.

The hypnotics and sedatives could broadly be classified into two main groups.

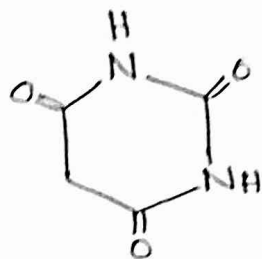
1. Barbiturates
2. Non-barbiturates

## 1. Barbiturates:

This is a general term used for derivatives of barbituric acid. This group comprises of barbiturates, ureid derivatives and some related ureides.

Example: glutethimide, methyl pryro.

These are derivatives of barbituric acid which is obtained as a condensation product of urea and malonic ester.



Barbituric acid.

Barbituric acid itself does not have any sedative or hypnotic properties but its substituent derivatives like 5-alkyl or aryl substituent shows hypnotic and sedative activity.

The substituted forms of barbituric acid are colourless, odourless crystalline solids. These are sparingly soluble in water and has a bitter taste. They are dissolved readily in organic solvents.

They are classified according to their duration of action into three types.

Types:-

- a) Long action 8 hours or more example: barbitone, methobarbitone
- b) Intermediate action 4 to 8 hours example:- amylbarbitone.
- c) Short action (less than 4 hours) example:- hexobarbitone, secobarbitone
- d) Ultra short action example:- thiopentone, methohexitone.

Therapeutic Uses of Barbiturates:-

They are used as sedatives. They are used to relieve tension, anxiety and are also used as in hypertension, peptic ulcer.

They are used as hypnotics. These are used for inducing sleep.

These are also used as anticonvulsants.

Barbiturates also used as preanaesthetic medication and general anaesthetics.

Glutethimide:-

It is absorbed from the gastrointestinal tract and is metabolized in the body. It is used as an hypnotic and its hypnotic effect start in about 30 minutes and it is long lasting. The drug is capable of inducing drug dependence.

Methyprylone:-

It is chemically related to glutethimide and is used as hypnotic drugs and its effective dose is about 200-400mg at bed time.

## 2. Non-Barbiturates:

There are several compounds which do not have barbiturate structure but they possess sedative and hypnotic effects.

Some important non-barbiturates are

- Alcohols example: ethanol, methyl paralytol
- Aldehydes example: paraldehyde
- Acetylates carbionals example: ethylchlorvynol ethinamate
- Benzodiazepines
- Inorganic ions Example: Bromide
- Miscellaneous Example: Methaqualone, Scopolamine

### a) Alcohols:-

Ethanol, chloral hydrate, trichloromethyl phosphate are used as sedative and hypnotics.

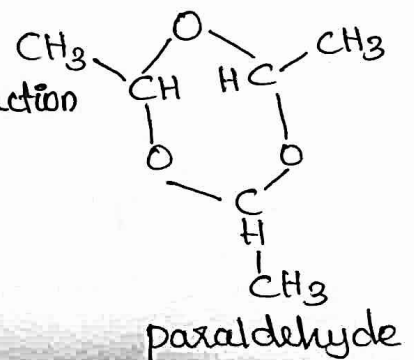
### b) Aldehydes:-

Paraldehyde:- It is a trimer of acetaldehyde. Chemically it is 2,4,6 trimethyl 1,3,5 trioxane.

It is administered either orally or injection forms. It is irritant to gastric mucosa.

It is used as mild analgesic effect.

It is useful anticonvulsant drug.



### c) Acetylated Carbinols:

Ethylchlorvynol: It is an oily liquid and is used for its hypnotic and sedative effects. It is generally administered orally in capsule forms.

### d) Benzodiazepines:

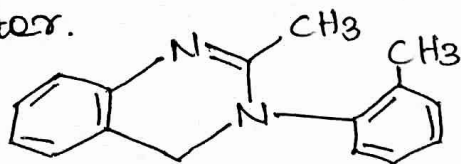
These are a composed system of a benzene ring fused with a seven membered ring having two nitrogen atoms and double bonds. These are named as 1,4 benzodiazepine according to the position of nitrogen at position 1 and 4.

### e) Inorganic ions:

Bromides: Bromides are not much in use now a days because of its adverse side effects such as conjunctivitis, headache, gastric distress, neurological disturbances.

### f) Miscellaneous Agents:

Methaqualone: It is a white crystalline powder which is insoluble in water.



Methaqualone

It has hypnotic effect that of short action barbiturates. It also used in antitussive, local anaesthetic.

## Tranquilizers

The tranquilizers have been defined as drugs which give "peace of mind" without causing hypnosis or anaesthesia. Originally the term tranquilizer was used to describe the psychic effect of reserpine and chlorpromazine which have the ability to calm a patient suffering from psychotic disorders.

- I. Antipsychotic drugs (Major tranquilizers)
- II. Anti anxiety drugs (Minor tranquilizers)

### I. Antipsychotic drugs:

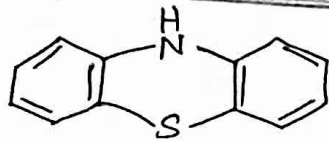
The antipsychotic drugs mainly consist of dopamine receptors, antagonists.

Antipsychotics are considered as major tranquilizers except for a few newly developed drugs. The major use of antipsychotics is to treat schizophrenia and other psychiatric and organic disorders.

These drugs are further classified as

#### 1. Phenothiazines:

All the phenothiazines have the same three ring phenothiazine nucleus but differ in the side chains joined to the nitrogen atom of the middle ring.



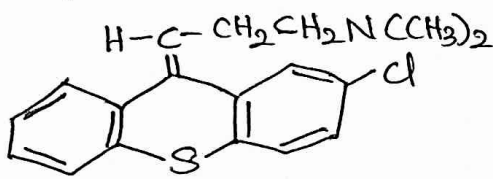
phenothiazine nucleus

These drugs are typed according to the aliphatic, piperazine, piperidine nature of the side chain.

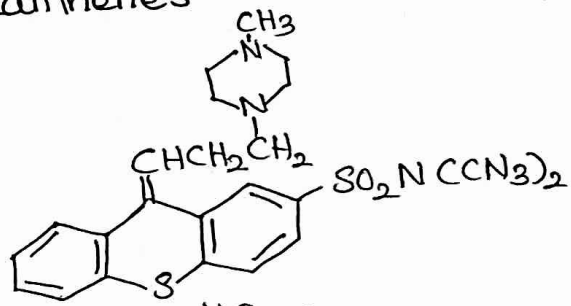
## 2. Thioxanthenes:

The thioxanthene three ring nucleus differs from the phenothiazine nucleus by the substitution of a carbon atom for the nitrogen atom in the middle ring.

The two available thioxanthenes have either aliphatic or a piperazine side chain.



chlorprothixene



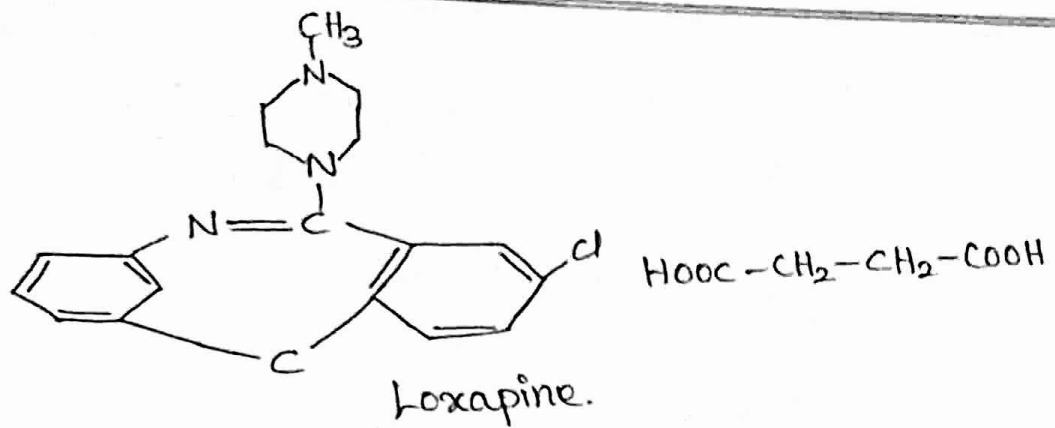
Thiothixene

These are useful drugs for the treatment of schizophrenia.

## 3. Dibenzoxazepines:

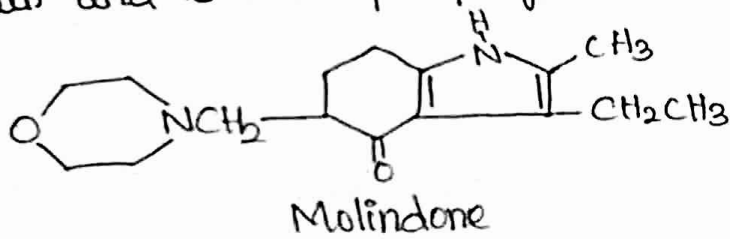
The chemical structure of these drugs are based on another modification of the three ring phenothiazine nucleus. loxapine is a drug belonging to this group which has a piperazine sidechain.

This drug is used in schizophrenies, organic brain psychoses, psychotic depressions.



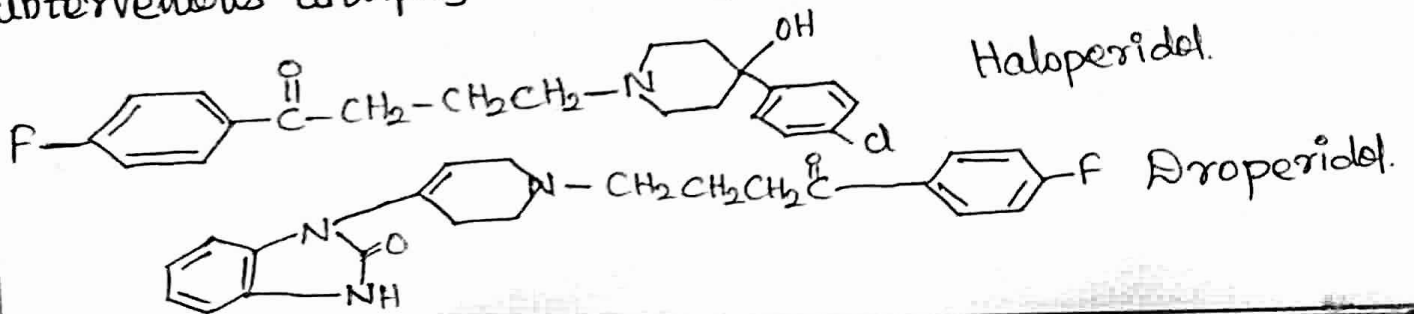
#### 4. Dihydroindoles:

The example of the drug belonging to this group is molindone. This drug has some unusual properties such as not inducing weight gain and is less epileptogenic than the phenothiazines.



#### 5. Butyrophenones:

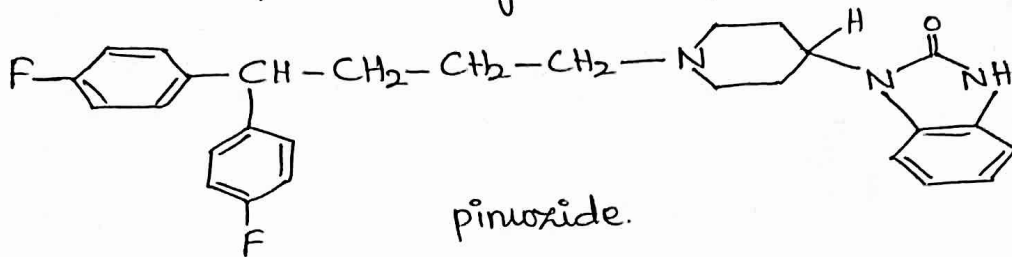
Example of the drugs are Haloperidol and Droperidol. Haloperidol is most widely used antipsychotic drug. Droperidol is used as an adjuvant in anaesthesia and sometimes it is used as intravenous antipsychotic drug in emergencies.





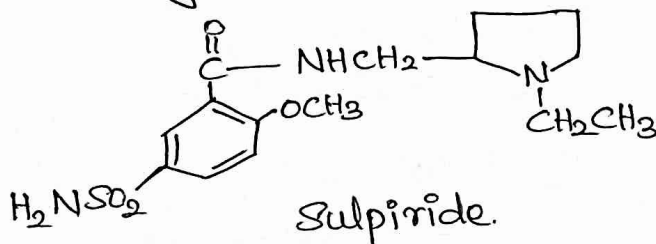
## 6. Diphenylbutylpiperidines:

These drugs are structurally similar to butyrophenones. The most important drug of this group is pimozide.



## 7. Benzamides:

Example of drug is sulpiride. It is an effective antipsychotic drug with fewer neurological side effects.



## Adverse Effect of Antipsychotic Drugs:

These drugs cause postural hypertension, cause peripheral anticholinergic effects like dry mouth and nose, blurred vision, constipation, urinary retention.

These drugs can cause cardiotoxic effects, weight gain, skin eruptions. Phenothiazines pass into breast milk.

## II. Antianxiety Drugs:-

These drugs are used to relieve anxiety and are also known as "minor tranquilizers". These drugs also exhibit sedative and hypnotic properties when given in adequate doses.

Antianxiety drugs can be classified as

### 1. Benzodiazepines:-

These drugs are usually effective in moderate doses have a wide margin of safety and are long acting. All of the benzodiazepines are similar in chemical structure and clinical properties. These drugs are marked as minor tranquilizers and are used for the treatment of anxiety.

Adverse effect: Ataxia, hypotension, excessive doses can cause coma, disinhibition, dysarthria.

### 2. Non-benzodiazepines:-

Some important drugs are chloralhydrate, Buspirone  
Adrenergic blocking agents.

Chloralhydrate: Its chemical structure is  $\text{CCl}_3\text{CH}(\text{OH})_2$ .  
It is one of the oldest sedative hypnotic drug which is used in the treatment of anxiety.

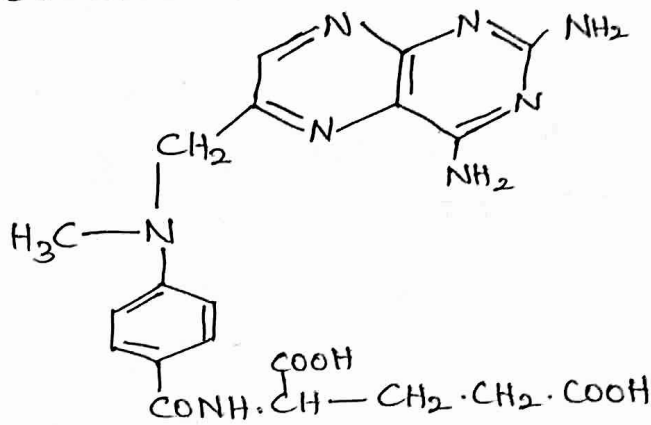
Adverse effect: nausea, vomiting, diarrhea, hepatic renal damage. It should not be used during pregnancy.

It is effective against malignant cells of lymphoid series. It is administered orally and is available as drug tablets. This drug is used in the treatment of chronic lymphocytic leukaemia. It is used in autoimmune disorders.

Adverse effects:- Gastrointestinal irritation, bone marrow depression with leukopenia.

(ii) Methotrexate:-

It is an antimetabolite of folic acid and has the adjoining structure.



Methotrexate.

This drug acts on the bone marrow. It is used acute lymphatic leukaemia especially in children. This drug can be administered in the form of injection or tablets.

Adverse effect:- megaloblastic anaemia, intestinal ulceration, diarrhoea, liver damages.

## Diabetes and Hypoglycemic Drugs

Diabetes is a disease of metabolism due to deficiency of insulin. Blood sugar level is maintained constant at a value of 70-120 mg of glucose/100ml. Though several hormones are involved in the maintenance of diabetes the most important ones are insulin and glucagon.

Diabetes are two types

(i) Diabetes insipidus:

This diabetes arise due to lesser secretion of Vasopressin by posterior pituitary gland.

(ii) Diabetes mellitus:-

This type of diabetes arises by the deficiency of insulin and the blood sugar level rise more than normal.

Diabetes mellitus are of two types

a) Juvenile

b) Adult type.

Juvenile diabetes mellitus is hereditary and is treated by giving insulin.

Adult type occurs in elderly people and is treated by controlling the diet and oral antidiabetic drug should be given.

## Oral Hypoglycaemic Agents:

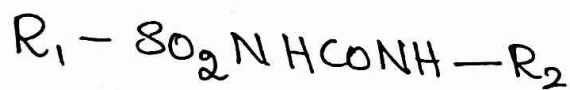
Insulins are ineffective through oral administration and hence oral hypoglycaemic drugs were introduced with cold control diabetic when administered orally. An ideal antidiabetic drug should be effective by mouth, non toxic and correct the basic metabolic defects in diabetes.

The most important drug belongs to two groups

- (1) Sulphonylureas
- (2) Biguanides

### 1) Sulphonylureas:

These drugs are chemically related to sulphonamide and have a basic structure



(basic structure of sulphonyl urea drugs)

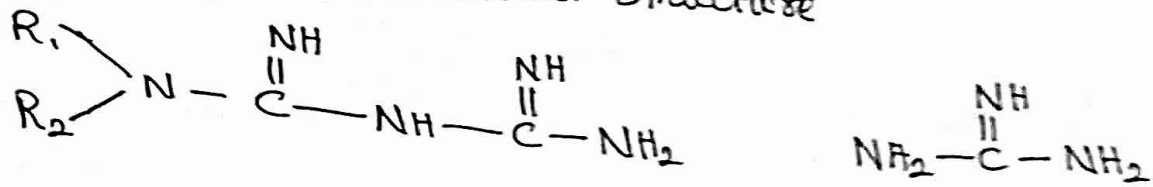
2) Sulphonyl ureas are useful in treating diabetes who can not be controlled by diet alone.

Some important drugs of this group

- i) Tolbutamide
- ii) Chlorpropamide
- iii) Glibenclamide
- iv) Tolazamide.

## 2) Biguanides:-

When two guanide molecules are joined together through a common -NH- link it is known as biguanides and their general chemical structure



General structure of Biguanides.

Though these drugs are not used in treating juvenile diabetes but it is used along with insulin to control juvenile diabetic.

Some important example of biguanides:-

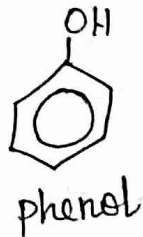
- i) Phenformin
- ii) Metformin.

## Anti-Septics and Disinfectants

Antiseptics and disinfectants are the chemical substance which are used to kill or inhibit the growth of pathogenic micro-organism.

An ideal-antiseptic and disinfectant agent should have a wide antimicrobial spectrum and should destroy bacteria, viruses, spores, protozoa, fungi.

### 1. Phenols:-



It is a potent bactericidal and fungicidal agent and acts by denaturing the bacterial proteins. Hence it is called a general proto-plasmic poison injuring the micro-organism and the cells of the body tissue.

It causes severe gastrointestinal corrosion, pain, vomiting, shock may cause become fatal.

### 2. Halogen compounds:-

Halogen and halogen compounds are extensively used as disinfectants and antiseptics.

Chlorine exerts a bactericidal action against a variety of gram positive and gram negative organisms in very low concentration.

Some important halogen compounds:

- i) chloramines
- ii) Haloxone
- iii) Chlorinated lime.

3 Dyes:

Natural dyes have been replaced by more stable synthetic dyes and these are used as antiseptics chemotherapeutics, colouring agents.

Some important dyes:

- i) Crystal violet
- ii) Methylene blue
- iii) Brilliant green.