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CONTENT TYPE	Notes
SEARCH KEY WORD	Introduction of hypnotic and sedative , Introduction of tranquilizers

(CONTENTCREATER/TEACHER)

Course Content:

UNIT	CONTENTS
UNIT-2	Hypnotic and sedative and tranquilizers: detail of compounds.

UNIT 2nd

HYPNOTIC AND SEDATIVE

Hypnotics are the drugs which produce sleep and so are used in cases of insomnia (sleeplessness). Sedatives are drugs which reduce excitement and cause sedation. The same drug may act as a hypnotic or sedative or both depending upon the dose. Hypnotic and sedatives depress the central nervous system for producing sleep and sedation.

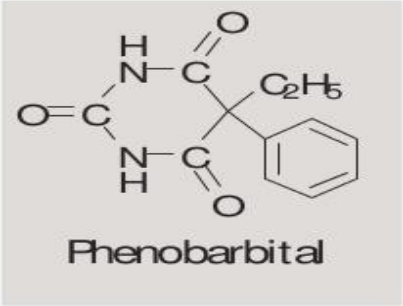
CLASSIFICATION OF SEDATIVE AND HYPNOTIC:-

a) **Barbiturates**
   Phenobarbitone
   Butobarbitone
   Cyclobarbitone
b) **Aldehyde**
   Paraldehyde
c) **Benzodiazepines**
   Nitrazepam
d) **Miscellaneous**
   Methyprylone
   Glutethimide
   Triclofos sodium

Phenobarbitone

Phenobarbitone is a long acting barbiturate. It is a derivative of barbituric acid and its structure has been given below.

Phenobarbital



- **Barbiturate drug**, trade name **Luminal**
- **Mainly as Anticonvulsant**
- Hypnotic effect, Sedative effect,
- Bioavailability after **proper administration** = 95%
- Metabolism= Hepatic (Cytochrome P450)
- Half-life= 53-118 hours
- Excretion= Renal and Fecal

Physical properties :-

Colour:- Colourless crystals or occurs as white crystalline powder

Odour:- Odourless

Taste:- Bitter taste

Solubility:- It is very slightly soluble in water and soluble in ethanol and ether spalingly soluble in chloroform .

Chemical properties:-

1) When phenobarbione is dissolved in ethanol and one drop of cobalt chloride solution and one drop of dilute ammonia solution are added, a violet colour is produced.
2) When phenobarbitone and phenobarbitone sodium is dissolved in methanol and a mixture of cobaltous chloride and calcium chloride solutions is added to this solution and then after mixing and shaking , dilute sodium hydroxide solution is added , a violet-blue colour and a precipitate are produced.

Stability and Storage :-

The compound may be affected by carbon dioxide of the atmosphere, store them I tightly closed container.

Uses:-

1) It is mainly used as an anticonvulsant and seldom used as sedative and hypnotic .

2) It is used to treat grant mal and status epilepticus.

3) It is a valuable antiepileptic drug.

4) It is also used to prevent withdrawal symptoms in people who are dependent on another barbiturate medication and going to stop taking the medication.

5) It is also used to relief anxiety.

Official:-

Phenobarbitone, I.P,B.P

Phenobarbitone Tablets,I.P,B.P

Phenobarbitone Sodium I.P,B.P

Phenobarbitone Sodium Injection I.P

Phenobarbitone Sodium Tablets I.P,B.P

Phenobarbitone Elixirs ,B.P

Brand name:-

For Phenobarbitone:- Gardenal, Luminal, Dormiral, Euneryl,Somonal

For Phenobarbitone Sodium:-Gardenal sodium, Luminal sodium, Sol Phenobarbitone etc.

Butobarbitone

This compound has the same structure as barbitone but differs from it in having a n-butyl group in place of one of the ethyl groups at the 5^{th} position.

Physical properties :-

Colour:- Colourless crystals or occurs as white crystalline powder

Odour:- Odourless

Taste:- Bitter taste

Solubility:- It is very slightly soluble in water and soluble in etherand freely soluble in ethanol and chloroform . It dissolves in and forms water-soluble compounds with alkali hydroxides and alkali carbonates and also with ammonia .

Chemical properties :-

If Butobarbitone is dissolved in methanol and a mixture of cobaltous chloride and calcium chloride solutions is added to this solution and then after mixing and shaking , dilute sodium hydroxide solution is added , a violet-blue colour precipitate are produced.

Stability and storage:-

It should be store in well-closed containers.

Uses:-

1) It is used as a sedative and hypnotic.

2) It is used to relieve anxiety, nervous tension and insomnia

Official:-

Butobarbitone, B.P

Brand names:- Soneryl, Neonal, Etoval,Butobarbital etc.

Cyclobarbitone

Cyclobarbitone contains in addition to the ethyl group, a cyclohexenyl group. So it is 5-ethyl-5-cyclohex-1-enylbarbituric acid.

Physical properties :-

Colour:- Cyclobarbitone sodium is white or slightly yellowish,crystalline powder

Odour:- Characterstic

Taste:- Bitter taste

Melting point:- 171-174˚C

Solubility:- It is very slightly soluble in cold water and more soluble in hot water , alcohol and ether.

Chemical properties:-

If a small quantity of the Cyclobarbitone calcium is added to a mixture of vanillin in alcohol, sulphuric acid and water , shaken and allowed to stand for 5 minutes, a greenish-yellow colour is formed slowly. It becomes dark red when it is heated on a water bath for 10 minutes.

Stability and storage:-

It should be store in an airtight containers .

Uses:-

1) It is used as a sedative and hypnotic.

2) It is used to treat insomnia.

Official:-

Cyclobarbitone calcium,B.P.

Brand names:-

For Cyclobarbitone:- Sonaform, Hexemal,Cyclodorm,Phanadorm etc

For Cyclobarbitone calcium:- Pronox,Hexemal calcium,Itridal,Cyclobarbital calcium .

Paraldehyde:-

Paraldehyde is a polymer of acetaldehyde. It is a trimer and consists of three molecules of acetaldehyde.

Physical properties :-

Colour:- Transparant,colourless or pale yellow liquid

Odour:- Characterstic

Taste:- Unpleasant taste

Boiling point:- 123-126˚C

Solubility:- It is soluble in water but less soluble in boiling water.It is miscible with ethanol, ether, chloroformand volatile oil.

Chemical properties:-

If ammonical silver nitrate is added to a solution of paraldehyde and heated on a water bath, silver is deposited as a mirror on the side of the test tube .

Stability and storage:-

It is easily oxidised to acetic acid , paraldehyde should be kept in a small,well-filled,airtight container , protected from light and stored at a low temperature.

Uses:-

1) It is a powerful hypnotic with a short,lasting action.
2) It has no analgesic or anticonvulsant action, it is able to control certain convulsions because of strong CNS depression.

Official:-
Paraldehyde ,I.P,B.P.
Paraldehyde Injection ,B.P.

Brand names:-paraldehyde, Paracetaldehyde.

Nitrazepam:-

Nitazepam is a benzodiazepine derivative . Benzo-diazepine is formed by the fusion of one benzene ring and one diazepine ring which is a 7-membered ring containing two nitrogen atoms.

Physical properties :-

Colour:- Yellow , crystalline powder

Odour:- Odourless

Melting point:- 226˚C

Solubility:- It is practically insoluble in water , slightly in ethanol and ether and sparingly soluble in chloroform.

Chemical properties.

1) If nitrazepam is dissolved in methanol and dilute sodium hydroxide solution is added an intense yellow colour is produced.
2) Nitrazepam contains a nitro group on the benzene ring, it can be reduced to amino group and diazotised by adding hydrochloric acid and sodium nitrite.This after adding sulpharnic acid ,can be coupled with N-(naphthyl) ethylenediamine hydrochloride to give a red colour.

Stability and storage :-

It is affected by light, store it in well-closed ,light-resistant containers.

Uses

Hypnotic. It is a long – acting hypnotic with good sedation**.**

Official

Nitrazepam,I.P.,B.P.
Nitrazepam,Tablets,I.P.,B.P.
Nitrazepam Capsules,B.P
Nitrazenpam Oral Suspension,B.P.

Brand names

Sedamas, Hypnotex, Nirven e.

Methyprylone

Methyprylone is a derivative of 2,4- piperidinedione.

Physical properties :-

Colour:- White crystalline powder

Odour:- characteristic

Melting point:- 76-77˚C

Taste:- Bitter

Solubility:- It is soluble in water. It is soluble in alcohol,ether,benzene andchloroform.

Stability and storage:-

Store in well-closed containers.protected from light .

Uses:-

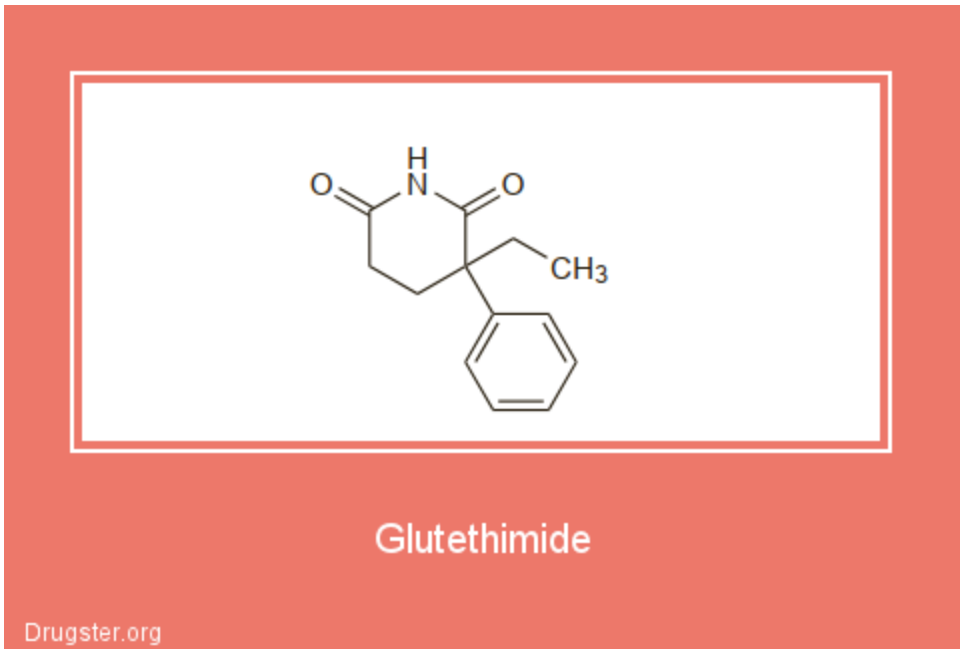
Hypnotic .It acts Like glutethimide .it is not official in the latest I.P.or B.P.

Brand name:-

Noludar , Noctan, Dimerin,

Glutethimide

Glutethimide is also a derivative of 2,6- piperidinedione.



Physical properties :-

Colour:- White or almost white powder or as colourless crystals.

Melting point:- 86 to 89˚C

Solubility:- It is practically insoluble in water ,freely soluble in alcohol ,soluble in ether and very soluble in dichloromethane .

Chemical properties:-

If the substance is dissolved in methanol and a cooled mixture of formalin and concentrated sulphuric acid is added and heated on a water bath , the solution becomes red and exhibits an intense blue fluorescence under ultraviolet light ,that is at 365 nm.

Stability and storage:-

Store in well-closed containers, protected from light.

Uses:-

It was considered to be a safe non-barbiturate hypnotic .but later on it was found that it had all the disadvantage of barbiturates .so it is not very much used nowadays.

Official :-

Glutethimide ,B. P.

Brand name:-

Doriden,Elrodorm**.**

Triclofos sodium

Triclofos sodium is 2,2,2-trichloroethanol sodium dihydrogen phosphate

Physical properties :-

Colour:- White or almost white powder

Odour:- Odourless

PH:- 3-4.5

Solubility:- It is practically insoluble in ether , slightly in ethanol and freely soluble in water.

Chemical properties:-

1) If triclofos sodium is oxidised by heating with acidified permanganate on a water bath and excess of permanganate is removed by adding oxalic acid and pyridine and sodium hydroxide solution are added and heated on a water bath , a pink colour is produced in the pyridine layer.
2) If triclofos sodium is dissolved in water,it decomposes liberating chloride ions. If silver nitrate solution is added, a white precipitate of silver chloride insoluble in ammonia and nitric acid is formed .

Stability and storage:-

It must be kept in a well-closed containers.

Uses:-

Hypnotic . It is less irritating and stable but rarely used.

Official:-

Triclofos sodium,B.P

Triclofos oral solution,B.P

Brand names:- Tricloryl,Triclos,Sodium trichlorofos.

TRANQUILIZERS

A tranquilizer refers to a drug which is designed for the treatment of anxiety,fear,tension,agitation ,and disturbances of the mind , specifically to reduce states of anxiety and tension .

Major tranquilizer :- might refer to antipsychotic .

Minor tranquilizer :- usually refers to anxiolytics.

Antipsychotics:-

Drug used to treat mental illness and mental disorders are also known as psychotropic drugs and psycho pharmacological agents. Mental disorders can be broadly divided in to neuroses, psychoses and personality disorders. Of these, psychoses may be treated with antipsychotics.

Classification of antipsychotics

1. Phenothiazines

a) Chlorpromazine

b) Prochlorperazine

c) Trifluoperazine

2. Ring analog of phenothiazine

a) Thiothixene

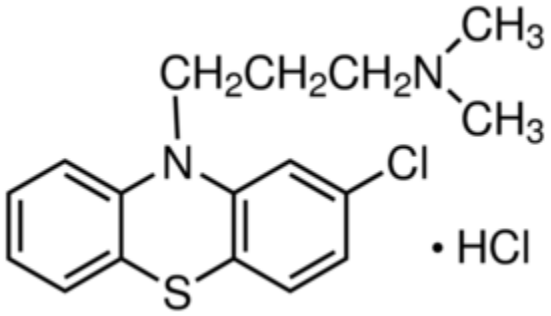
3. Butyrophenones

a) Haloperidol

b) Triperidol

1. Chlorpromazine :-

Chlorpromazine has a chlorine atom in the second position and a propyl group in the 10th position . The third carbon atom of the propyl radical carries a dimethyl amino group.



2-chloro-10-(3-dimethylaminopropyl) phenothiazine

Physical properties :-

Colour:- White or creamy white, crystalline powder

Odour:- Odourless

Taste:- Bitter taste

Melting point:- 194-198˚C

Solubility:- It is very soluble in water , freely soluble in ethanol,soluble in chloroform and practically insoluble in ether

pH:- 4

Chemical properties :-

1. If a small quantity of the substance is dissolve in water ,a cherry red colour is produced. It darkens slowly on standing . If this solution is divided into two parts and

one portion is warmed, it changes to brown and magenta.If decinormal potassium dichromate is added to the other portion , the colour change to brownish red.

2. In another test if ferric chloride solution is added to an aqueous solution of the substance , a stable red colour is produced.

Stability and storage :-

It is affected by air and light , store it in a tightly-closed, light-resistant container .

Uses :-

1. It has effective antipsychotic action and is used in the treatment of schizophrenia to control hyperkinetic states and addression .
2. It is also used an antiemetic and used in the treatment of nausea and vomiting and also intractable hiccup.

Official :-

Chlorpromazine hydrochloride I.P,B.P

Chlorpromazine hydrochloride injection I.P

Chlorpromazine oral solution B.P

Chlorpromazine hydrochloride tablets I.P

Brand name :-

Chlorpromazine, Largactil, Chloractil ,Torazine ,Taroctyl

2. Prochlorperazine

Prochlorperazine has almost the same structure as chlorpromazine . However the –N(CH3)2group attached to the end carbon atom end carbon atom of the propyl group at the 10^{th} position is replaced by a methyl piperazino group.

Physical properties :-

Colour:- White or pale yellow, crystalline powder

Odour:- Odourless

Solubility:- It is very slightly soluble in water and ethanol and practically insoluble in ether and chloroform

Chemical properties :-

Prochlorperazine maleate is triturated with water and sodium hydroxide solution and extracting with ether , thus removing the Prochlorperazine in ether .

One portion of the aqueous layer containing the sodium salt of malaeic acid is first treated with resorcinol and concentrated with sulphuric acid and heated on water bath . no colour is produced . however if another portion of the aqueous solution is first treated with bromine solution and heated on water bath , the maleic acid is oxidized to dibromosuccinic acid . If this solution is treated with resorcinol and concentrated sulphuric acid and heated on water bath ,a dye is produced which is indicated by the solution turning blue.

Stability and storage :- It is store in well closed container protect from light.

Uses :- It has the same effects as chlorpromazine but at lower doses.

Officials :-

Prochlorperazine Maleate , I.P,B.P

Prochlorperazine Maleate Tablets, I.P

Prochlorperazine Mesylate , I.P,B.P

Prochlorperazine Maleate Injection , I.P

Brand Name :- Stemetil, Nipodal , Tementin

3.Trifluoperazine

Trifluoperazine has the same structure as Prochlorperazine in the sense that it contains the same side chain at position 10. However it contains a trifluoromethyl group at position 2 in place of the chloro group in prochloroperazine.

Physical properties :-

Colour:- White or pale yellow, crystalline powder

Odour:- Odourless

Solubility:- It is freely soluble in water ,soluble in ethanol ,slightly soluble in chloroform

and practically insoluble in ether.

Chemical properties :-

If trifluoperazine hydrochloride is dissolved in concentrated sulphuric acid and allowed to stand for 5 minutes, an orange colour is produced.

a) An aqueous solution of the substance is first treated with bromine solution and shaken and concentrated sulphuric acid is added and shaken vigorously, a red colour is produced.

b) An aqueous solution of the substance is second treated with concentrated nitric acid , a dark red colour is produced . It finally becomes pale yellow .

Stability and storage :-

It is slightly hygroscopic and is also sensitive to light, store it in a well-closed, light-resistant container.

Uses :-It has the same actions and uses as chlorpromazine.

Official:-
Trifluoperazine hydrochloride I.P,B.P
Trifluoperazine hydrochloride Injection, I.P
Trifluoperazine hydrochloride Tablets I.P

Brand Name :- Espzine ,Trinicalm, Eskazine,Stelazine,Terfluzine.

4.Thiothixene

Thiothixene is a ring analog of chlorpromazine in that it is not derived from phenothiazine but from thioxanthene . It is used as the hydrochloride .

Physical properties :-

Colour:- White ,crystalline powder

Odour:- Slight odour

Solubility:- It is soluble in water , ethanol and chloroform,practically insoluble in ether and acetone .

Stability and storage :-

It is affected by light , store in well-closed containers protected from light.

Uses:-

It has the same uses as chlorpromazine as an antipsychotic .

It is very potent and its sedative action is less.

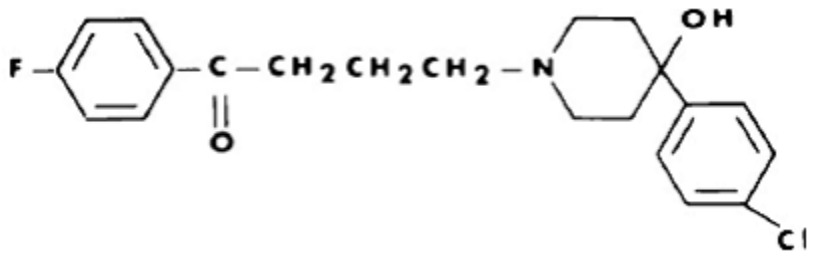
It is effective in both types of schizophrenia, that is in both depressed and agitated schizophrenia.

Official :- Thiothixene hydrochloride injection U.S.P

Brand names:- Tiotixene, orbinamon and navane .

5. Haloperidol

Haloperodol is a butyrophenone, that is the keto group is present between the phenyl radical and a propyl group.



Physical properties :-

Colour:- White or slightly yellowish , amorphous or crystalline powder

Odour:- Odourless

Melting point :- 150˚C

Solubility:- It is soluble in chloroform, sparingly soluble in ethanol and slightly soluble in ether and practically insoluble in water .

Chemical properties :-

a) If an alcoholic solution of haloperidol is treated with dinitrobenzene solution and 2M ethanolic potassium hydroxide , a violet colour is produced . it becomes brownish red after 20 minutes .
b) If an alcoholic solution of haloperidol is mixed with a mixture of alizarin red S solution and zinconylnitrate solution , the red colour of the solution becomes yellow .

Stability and storage :-

It is affected by light , store in air tight containers protected from light.

Uses :-

It is a powerful antipsychotic .its side effects are much less compared to the phenothiazines . it is used to treat acute schizophrenia and other diseases.

Officials :-

Haloperidol ,I.P,B.P

Haloperidol injection , I.P,B.P

Haloperidol oral solution I.P,B.P

Strong haloperidol oral solution ,B.P

Haloperidol oral solution I.P,B.P

Haloperidol tablets ,I.P,B.P

Brand name :- Serenace, hexidol,hexidol plus, aloperidine , brotopon, halidol,depidol.

Antianxiety agent (Anxiolytics)

Anxiety is an unpleasant mental state characterized by mental discomfort, a feeling of uneasiness and a vague fear of some unknown threat or danger. The antianxietydrugs

counteract these symptoms and produce a restful or peaceful state of mind without interfering with normal mental or physical function.

Classification of anxiolytic agents

a)Benzodiazipines:-
1.Chlordiazepoxide
2.Diazepam
3.Lorazepam
b)Miscellaneous:-
1.Meprobamate

1. Chlordiazepoxide

Chlordiazepoxide is a 1,4-benzodiazepine derivatives .

Physical properties :-

Colour:- White or light yellow , crystalline powder

Odour:- Odourless

Taste:- Bitter

Solubility:- It is sparingly soluble in ethanol and slightly soluble in ether and practically insoluble in water .

Chemical properties :-

The compound can be disintigrated by boiling with hydrochloric acid . the decomposition product answers the reaction of primary aromatic amines such as getting diazotised and copuled with α-naphthol or N-ethylene diamine dihydrochloride to give a red or reddish violet azo dye.

Stability and storage :-

It is affected by light, store in well-closed containers protected from light.

Uses :-

1. It act as a sedative and minor tranquilizer. It is slowly absorbed but its action is long lasting.

2. It is used to relieve anxiety and controlagitation caused by alcohol withdrawal.

Officials :-

Chlordiazepoxide , I.P,B.P

Chlordiazepoxide tablets, I.P,B.P

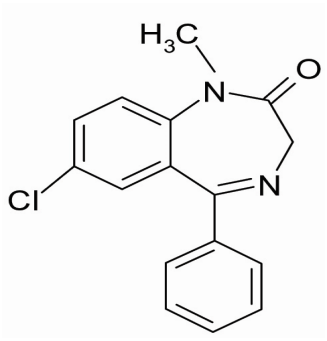
Chlordiazepoxide hydrochloride, B.P

Chlordiazepoxide capsules, B.P

Chlordiazepoxide hydrochloride tablets, B.P

Brand names:- Librium , equilibrium, mesricem,mesural etc

2. Diazepam

Diazepam is also a 1,4-benzodiazepine derivative. It has totally 4 double bond , three in the benzene ring and one in the diazepine nucleus. 

Physical properties :-

Colour:- White to pale yellow , crystalline powder

Odour:- Odourless

Melting point :- 131-135˚C

Solubility:- It is sparingly soluble in waterbut freely soluble in chloroformand soluble in ethanol.

Chemical properties :-

If diazepam is dissolved in sulphuric acid , the solution exhibits a greenish yellow flurorescence when examined under ultraviolet light.

Stability and storage :-

It is affected by light, store in well-closed containers , light-resistant containers.

Uses:-

1) It has anxiolytic, sedative, anticonvulsant, muscle relaxant and amnestic actions.
2) It is used in the control of muscle spasm of tetanus.

Officials:-

Diazepam, I.P,B.P

Diazepam Capsules, I.P,B.P
Diazepam Injection, I.P,B.
Diazepam oral solution, I.P,B.P
Diazepam tablets, I.P,B.P

Brand names :-, tranquase Valium, calmpose, levium etc.

3.**Lorazepam**

Lorazepam is also,4-benzodiazepines derivative which has almost the same structure as diazepam but has no methyl group at position I but has a hydroxyl group at position 3.

Physical properties :-

Colour:- White or almost white,crystalline powder

Odour:- Odourless

Melting point :- 166-168˚C

Solubility:- It is sparingly soluble in etanol and slightly soluble in chloroform and insoluble in water.

Stability and storage :-

It is store mild environmental temperatures and nonrefrigerated storage of the drug, light-resistant containers.

Uses:-

1) It is use to treat anxiety .

2) Lorazepan belongs to the class of drugs known as benzodiazepines which act on the brain and nerves to produce a calming effect .

3) This drugs works by enhancing the effect of a certain natural comical in the body.

Officials:-

Lorazepam,B.P
Lorazepam Injection,B.P
Lorazepam Tablets ,B.P

Brand names:- larpose ,ativam, calmase, lorax etc.

4. Meprobamate

Meprobamate is a relatively simple compound,being the biscarbamate of a diol .it is actually 2-methyl-2-n-propyl-1,3-propanediol dicarbamate .

Physical properties :-

Colour:- White or almost white, crystalline powder or amorphous powder

Odour:- Odourless

Taste:- characteristic bitter

Melting point :- 104-108˚C

Solubility:- It is slightly soluble in water and ether and freely soluble in ethanol.

Chemical property :- meprobamates answers a colors reaction in which it is dissolved in ethanolic potassium hydroxide and boiled .then glacial acetic and a solution of cobalt nitrate in absolute ethanol are added .A deep blue colour is produced.

Stability and storage :- it is store in airtight containers.

Uses:-

1) It is used as tablets and capsules in the treatment of anxiety and tension.

2) Meprobamate has selective effects at multiple sites with in the CNS , including the limbic system.

3) It has also inhibit multineuronal spinal reflexes.

4) It has mild tranquilinzing properties and some anticonvalsant and muscle-relaxant properties.

5) Meprobamate can produce several CNS abverse effects.

Officials:-

Meprobamate ,B.P.

Brand names :- Equanil,Miltown,Calmate ,Equinil etc.