COURSE FILE

Mrs. J. SUJATHA

BP402T-MEDICINAL CHEMISTRY-I

St.Pauls
College of Pharmacy
(Approved by AICTE, PCI and Affiliated to Osmania University)

COURSE FILE CONTENTS

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St. Pauls College of Pharmacy
Turkayamjal
R.R. Dist. 501 510

St.Pauls
College of Pharmacy
(Approved by AICTE, PCI and Affiliated to Osmania University)

CLASS	:	IV-SEM – SEC-A
COURSE	:	MEDICINAL CHEMISTRY-I
INSTRUCTOR NAME	:	Mrs.J.SUJATHA
EMAIL	:	sujathajadi25@gmail.com
CLASS ROOM	:	ROOM NO-8
CONTACT TIME	:	9AM-4.40PM

Table-IV: Course of study for semester IV

Course code	Name of the course	No. of hours	Tutorial	Credit points
BP401T	Pharmaceutical Organic Chemistry III– Theory	3	1	4
BP402T	Medicinal Chemistry I – Theory	3	1	4
BP403T	Physical Pharmaceutics II – Theory	3	1	4
BP404T	Pharmacology I – Theory	3	1	4
BP405T	Pharmacognosy and Phytochemistry I– Theory	3	1	4
BP406P	Medicinal Chemistry I – Practical	4	-	2
BP407P	Physical Pharmaceutics II – Practical	4		2
BP408P	Pharmacology I – Practical	4		2
BP409P	Pharmacognosy and Phytochemistry I – Practical	4	-	2
	Total	**31**	**5**	**28**

Prabhakar

ST.PAULS COLLEGE OF PHARMACY

Turkayamjal, Abdullapurmet, R.R. Dist.-501510

MEDICINAL CHEMISTRY – I (Theory)

SYLLABUS FOR B.PHARMACY IV Semester (2019-2020)

L:T:P (Hrs/Week): 3	SEE Marks: 75	Course Code: **BP402T**
Credits: 3	CIE Marks: 25	Duration of SEE: 3 Hours

COURSE OBJECTIVES	COURSE OUTCOMES
• Understand the chemistry of drugs with respect to their pharmacological activity • Understand the drug metabolic pathways, adverse effect and therapeutic value of drugs • Now the Structural Activity Relationship (SAR) of different class of drugs • Write the chemical synthesis of some drugs	**C402.1** Examine the relationship between various physicochemical properties of the drugs to their biological activity. **C402.2** Explain the significance of various biologically active scaffolds and their relation to biological activity. **C402.3** Infer the synthetic schemes and reactions involved in the synthesis of various drugs. **C402.4** Understand the concept of SAR and mechanism of action of various classes of drugs acting on ANS and CNS. **C402.5** Apply the medicinal chemistry knowledge of various classes of drugs for Drug design **C402.6** Identify structures of various antidotes in drug poisoning and their implications

B.PHARMACY PROGRAM OUTCOMES (PO'S)	
PO1	**Pharmacy Knowledge:** Possess knowledge and comprehension of the core and basic knowledge associated with the profession of pharmacy, including biomedical sciences; pharmaceutical sciences; behavioral, social, and administrative pharmacy sciences; and manufacturing practices.
PO2	**Planning Abilities:** Demonstrate effective planning abilities including time management, resource management, delegation skills and organizational skills. Develop and implement plans and organize work to meet deadlines.
PO3	**Problem analysis:** Utilize the principles of scientific enquiry, thinking analytically, clearly and critically, while solving problems and making decisions during daily practice. Find, analyze, evaluate and apply information systematically and shall make defensible decisions.
PO4	**Modern tool usage:** Learn, select, and apply appropriate methods and procedures, resources, and modern pharmacy-related computing tools with an understanding of the limitations.
PO5	**Leadership skills:** Understand and consider the human reaction to change, motivation issues, leadership and team-building when planning changes required for fulfillment of practice, professional and societal responsibilities. Assume participatory roles as responsible citizens or leadership roles when appropriate to facilitate improvement in health and well- being.
PO6	**Professional Identity:** Understand, analyze and communicate the value of their professional roles in society (e.g. health care professionals, promoters of health, educators, managers, employers,employees).
PO7	**Pharmaceutical Ethics:** Honour personal values and apply ethical principles in professional and social contexts. Demonstrate behavior that recognizes cultural and personal variability in values, communication and lifestyles. Use ethical frameworks; apply ethical principles while making decisions and take responsibility for the outcomes associated with the decisions.
PO8	**Communication:** Communicate effectively with the pharmacy community and with society at large, such as, being able to comprehend and write effective reports, make effective presentations and documentation, and give and receive clear instructions.
PO9	**The Pharmacist and society:** Apply reasoning informed by the contextual knowledge to assess societal, health, safety and legal issues and the consequent responsibilities relevant to the professional pharmacy practice.
PO10	**Environment and sustainability:** Understand the impact of the professional pharmacy solutions in societal and environmental contexts, and demonstrate the knowledge of, and need for sustainabledevelopment.
PO11	**Life-long learning:** Recognize the need for, and have the preparation and ability to engage in independent and life-long learning in the broadest context of technological change. Self-assess and use feedback effectively from others to identify learning needs and to satisfy these needs on an ongoing basis.

BP402 T Medicinal Chemistry I – Theory C210	CO1. Examine the relationship between various physicochemical properties of the drugs to their biological activity	3		2					2			1
	CO2. Explain the significance of various biologically active scaffolds and their relation to biological activity.	3							2			2
	CO3. Infer the synthetic schemes and reactions involved in the synthesis of various drugs.	2		1					1		1	2
	CO4. Understand the concept of SAR and mechanism of action of various classes of drugs acting on ANS and CNS.	2									1	1
	CO5. Apply the medicinal chemistry knowledge of various classes of drugs for Drug design	2		2					2		2	2
	CO6. Identify structures of various antidotes in drug poisoning and their implications	2		2					1		1	2

Prahlad

BP402T. MEDICINAL CHEMISTRY – I (Theory)

45 Hours

Scope: This subject is designed to impart fundamental knowledge on the structure, chemistry and therapeutic value of drugs. The subject emphasizes on structure activity relationships of drugs, importance of physicochemical properties and metabolism of drugs. The syllabus also emphasizes on chemical synthesis of important drugs under each class.

Objectives: Upon completion of the course the student shall be able to

1. understand the chemistry of drugs with respect to their pharmacological activity
2. understand the drug metabolic pathways, adverse effect and therapeutic value of drugs
3. know the Structural Activity Relationship (SAR) of different class of drugs
4. write the chemical synthesis of some drugs

Course Content:

Study of the development of the following classes of drugs, Classification, mechanism of action, uses of drugs mentioned in the course, Structure activity relationship of selective class of drugs as specified in the course and synthesis of drugs superscripted (*)

UNIT- I **10 Hours**

Introduction to Medicinal Chemistry

History and development of medicinal chemistry

Physicochemical properties in relation to biological action

Ionization, Solubility, Partition Coefficient, Hydrogen bonding, Protein binding, Chelation, Bioisosterism, Optical and Geometrical isomerism.

Drug metabolism

Drug metabolism principles- Phase I and Phase II.

Factors affecting drug metabolism including stereo chemical aspects.

UNIT- II **10 Hours**

Drugs acting on Autonomic Nervous System

Adrenergic Neurotransmitters:

Biosynthesis and catabolism of catecholamine.

Adrenergic receptors (Alpha & Beta) and their distribution.

Sympathomimetic agents: SAR of Sympathomimetic agents

Direct acting: Nor-epinephrine, Epinephrine, Phenylephrine*, Dopamine,

Methyldopa, Clonidine, Dobutamine, Isoproterenol, Terbutaline, Salbutamol*, Bitolterol, Naphazoline, Oxymetazoline and Xylometazoline.

- Indirect acting agents: Hydroxyamphetamine, Pseudoephedrine, Propylhexedrine.
- Agents with mixed mechanism: Ephedrine, Metaraminol.

Adrenergic Antagonists:

Alpha adrenergic blockers: Tolazoline*, Phentolamine, Phenoxybenzamine, Prazosin, Dihydroergotamine, Methysergide.

Beta adrenergic blockers: SAR of beta blockers, Propranolol*, Metibranolol, Atenolol, Betazolol, Bisoprolol, Esmolol, Metoprolol, Labetolol, Carvedilol.

UNIT-III **10 Hours**

Cholinergic neurotransmitters:

Biosynthesis and catabolism of acetylcholine.

Cholinergic receptors (Muscarinic & Nicotinic) and their distribution.

Parasympathomimetic agents: SAR of Parasympathomimetic agents

Direct acting agents: Acetylcholine, Carbachol*, Bethanechol, Methacholine, Pilocarpine.

Indirect acting/ Cholinesterase inhibitors (Reversible & Irreversible): Physostigmine, Neostigmine*, Pyridostigmine, Edrophonium chloride, Tacrine hydrochloride, Ambenonium chloride, Isofluorphate, Echothiophate iodide, Parathione, Malathion.

Cholinesterase reactivator: Pralidoxime chloride.

Cholinergic Blocking agents: SAR of cholinolytic agents

Solanaceous alkaloids and analogues: Atropine sulphate, Hyoscyamine sulphate, Scopolamine hydrobromide, Homatropine hydrobromide, Ipratropium bromide*.

Synthetic cholinergic blocking agents: Tropicamide, Cyclopentolate hydrochloride, Clidinium bromide, Dicyclomine hydrochloride*, Glycopyrrolate, Methantheline bromide, Propantheline bromide, Benztropine mesylate, Orphenadrine citrate, Biperidine hydrochloride, Procyclidine hydrochloride*, Tridihexethyl chloride, Isopropamide iodide, Ethopropazine hydrochloride.

UNIT- IV **08 Hours**

Drugs acting on Central Nervous System

A. Sedatives and Hypnotics:

Benzodiazepines: SAR of Benzodiazepines, Chlordiazepoxide, Diazepam*, Oxazepam, Chlorazepate, Lorazepam, Alprazolam, Zolpidem

Barbiturtes: SAR of barbiturates, Barbital*, Phenobarbital, Mephobarbital, Amobarbital, Butabarbital, Pentobarbital, Secobarbital

Miscelleneous:

Amides & imides: Glutethmide.

Alcohol & their carbamate derivatives: Meprobomate, Ethchlorvynol.

Aldehyde & their derivatives: Triclofos sodium, Paraldehyde.

B. Antipsychotics

Phenothiazeines: SAR of Phenothiazeines - Promazine hydrochloride, Chlorpromazine hydrochloride*, Triflupromazine, Thioridazine hydrochloride, Piperacetazine hydrochloride, Prochlorperazine maleate, Trifluoperazine hydrochloride.

Ring Analogues of Phenothiazeines: Chlorprothixene, Thiothixene, Loxapine succinate, Clozapine.

Fluro buterophenones: Haloperidol, Droperidol, Risperidone.

Beta amino ketones: Molindone hydrochloride.

Benzamides: Sulpieride.

C. Anticonvulsants: SAR of Anticonvulsants, mechanism of anticonvulsant action

Barbiturates: Phenobarbitone, Methabarbital. **Hydantoins:**

Phenytoin*, Mephenytoin, Ethotoin **Oxazolidine diones:**

Trimethadione, Paramethadione **Succinimides:**

Phensuximide, Methsuximide, Ethosuximide* **Urea and**

monoacylureas: Phenacemide, Carbamazepine*

Benzodiazepines: Clonazepam

Miscellaneous: Primidone, Valproic acid , Gabapentin, Felbamate

UNIT – V **07 Hours**

Drugs acting on Central Nervous System

General anesthetics:

Inhalation anesthetics: Halothane*, Methoxyflurane, Enflurane, Sevoflurane, Isoflurane, Desflurane.

Ultra short acting barbitutrates: Methohexital sodium*, Thiamylal sodium, Thiopental sodium.

Dissociative anesthetics: Ketamine hydrochloride.*

Narcotic and non-narcotic analgesics

Morphine and related drugs: SAR of Morphine analogues, Morphine sulphate, Codeine, Meperidine hydrochloride, Anilerdine hydrochloride, Diphenoxylate hydrochloride, Loperamide hydrochloride, Fentanyl citrate*, Methadone hydrochloride*, Propoxyphene hydrochloride, Pentazocine, Levorphanol tartarate.

Narcotic antagonists: Nalorphine hydrochloride, Levallorphan tartarate, Naloxone hydrochloride.

Anti-inflammatory agents: Sodium salicylate, Aspirin, Mefenamic acid*, Meclofenamate, Indomethacin, Sulindac, Tolmetin, Zomepriac, Diclofenac, Ketorolac, Ibuprofen*, Naproxen, Piroxicam, Phenacetin, Acetaminophen, Antipyrine, Phenylbutazone.

St. Pauls College of Pharmacy

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B. Pharm IV Sem Sec A Time Table - PCI
AY: 2019-2020

Day	09.00 AM TO 10.00 AM	10.00 AM TO 11.00 AM	11.10 AM TO 12.10PM	12.10PM TO 01.10PM	01.10PM TO 01.40AM	01.40 PM TO 02.40PM	02.40PM TO 03.40PM	03.40PM TO 04.40PM
MON	PH. COLOGY-I BATACH-I/ PH. COGNOSY BATCH-II				LUNCH	MC-I	PH. COGNOSY	POC-III(T)
TUE	POC-III	PH. COLOGY	POC-III	LAB		PP-II BATCH-I / MC-I BATCH-II		
WED	PP-II	LIBRARY	MC-I	PH. COGNOSY		PH. COLOGY	POC-III	PP-II (T)
THU	LIBRARY	PH. COGNOSY	PH. COLOGY(T)	LAB		PP-II BATCH-II / MC-I BATCH-I		
FRI	MC-I	PP-II	PH. COLOGY	LIBRARY		MC-I (T)	PP-II	PH. COGNOSY (T)
SAT	PH. COLOGY-I BATACH-II / PH. COGNOSY BATCH-I					CLUB ACTIVITIES/GUEST LECTURES		

PHARMACEUTICAL ORGANIC CHEMISTRY-III :Mrs. SHITAL SHIRIRANG DANGE

MEDICINAL CHEMISTRY-I : Mrs. J. SUJATHA (T+P)/ Mr L PRAVEEN(P)

PHYSICAL PHARMACEUTICS-II : Mrs T LAVANYA(T+P)/Ms.B. JYOTHI(P)

PHARMACOLOGY-I : Dr. NASREEN SULTANA (T+P)/ Mr P SUDHAKAR(P)

PHARMACOGNOSY : Dr. S. VANITA SAGAR (T+P)/ Mr A SANTHOSH(P)

Principal

St. Pauls College of Pharmacy
Turkayamjal (V), Abdullapurmet (M), R.R. Dist.
Course Plan
Program/Year/Sem: B.Pharmacy- IV sem
Academic Year: 2020-2021

SUBJECT: MEDICINAL CHEMISTRY-I **Name of the Faculty: Mrs. J. Sujatha**

S. No.	Week	Topic	Reference
UNIT-I			
1	1	Introduction to Medicinal Chemistry	1
2		History and development of medicinal chemistry	1
3		Ionization, Solubility, Partition Coefficient, Hydrogen bonding.	1
4		Protein binding, Chelation, Bioisosterism, Optical and Geometrical isomerism.	1
5	2	Drug metabolism	1
6		Drug metabolism principles- Phase I	1
7		Drug metabolism principles- Phase II	1
8		Factors affecting drug metabolism	1
9		Class test-I	
UNIT-II			
10	3	Adrenergic Neurotransmitters	1,2
11		Biosynthesis and catabolism of catecholamine	1,2
12		Adrenergic receptors	1
13		Sympathomimetic agents	1
14		SAR of Sympathomimetic agents	1
15	4	Adrenergic Antagonists- Alpha adrenergic blockers	1
16		Beta adrenergic blocker	1
17		SAR of beta blockers *	1
18		Propranolol, Atenolol	1,2
19		Class test-II	
UNIT-III			
20	5	Cholinergic neurotransmitters- Biosynthesis and catabolism of acetylcholine.	1,3
21		Parasympathomimetic agents: SAR of Parasympathomimetic agents	3
22		Direct acting agents- Carbachol	1
23		Indirect acting/ Cholinesterase inhibitors- Neostigmine	1,2
24	6	Cholinergic Blocking agents: SAR of cholinolytic agents	1
25		Solanaceous alkaloids and analogues- Ipratropium bromide	1
24		Synthetic cholinergic blocking agents- Dicyclomine hydrochloride	1
26		Procyclidine hydrochloride	1

27		Class test-III	
UNIT-IV			
28	7	Drugs acting on Central Nervous System	1
29		A. Sedatives and Hypnotics- Benzodiazepines- Diazepam	1,3
30		Barbiturtes: SAR of barbiturates, Barbital, Amobarbital	3
31		B. Antipsychotics- Phenothiazeines: SAR of Phenothiazeines	3
32		Promazine hydrochloride	1,2
33	8	Beta amino ketones, Benzamides	3
34		C. Anticonvulsants: SAR of Anticonvulsants	3
35		Barbiturates, Hydantoins, Ethosuximid	3
36		Benzodiazepines: Clonazepam	3
37		Class test-IV	
UNIT-V			
38	9	Drugs acting on Central Nervous System- General anesthetics	1
39		Inhalation anesthetics: Halothane	1
40		Dissociative anesthetics: Ketamine hydrochloride	1
41		Narcotic and non-narcotic analgesics	1
42		Methadone hydrochloride	1
43		Propoxyphene hydrochloride, Pentazocine, Levorphanol tartarate	1
44	10	Morphine and related drugs: SAR of Morphine analogues	1
45		Narcotic antagonists	1
46		Nalorphine hydrochloride, Levallorphan tartarate	1
47		Anti-inflammatory agents- Mefenamic acid	1
48		Ketorolac, Ibuprofen, Naproxen	1
49		Acetaminophen, Antipyrine, Phenylbutazone	1
50		Class test-V	

References:

1. Wilson and Giswold's Organic medicinal and Pharmaceutical Chemistry.
2. Foye's Principles of Medicinal Chemistry.
3. Burger's Medicinal Chemistry, Vol I to IV.

HOD

PRINCIPAL

METHOD OF TEACHING AND LECTURES NOTES

COURSE CONTENT	METHOD OF TEACHING
UNIT-I	
Physicochemical properties in relation to biological action	Chalk and board
Drug metabolism	Chalk and board
UNIT-II	
Adrenergic Neurotransmitters	Chalk and board
Adrenergic Antagonists	Chalk and board
UNIT-III	
Cholinergic neurotransmitters	Chalk and board
Cholinergic Blocking agents	Chalk and board
UNIT- IV	
A. Sedatives and Hypnotics	Chalk and board
B. Antipsychotics	Chalk and board
C. Anticonvulsants	Chalk and board
UNIT-V	
General anesthetics	Chalk and board
Anti-inflammatory agents	Chalk and board

Introduction to Medicinal Chemistry UNIT-I

Definition

According to the Recommendations of IUPAC — It concerns with the discovery, the development, the identification and the interpretation of mode of action at the molecular level

The study of Medicinal Chemistry involves

1. Synthesis
2. SAR — Structure activity relationship
3. Receptor interactions
4. Absorption, Distribution, Metabolism and excretion.
5. Therapeutic implications.
6. Important Adverse effects of the drugs / Toxicity.

Importance

* It describes the functional groups present in the drug and their relation to the rest of the molecule. This helps us to know which part of molecule contributes to the medicinal effects and suitable alterations can be done for better effect.

* It helps to differentiate which stereo-isomeric forms are effective for the treatment. The organic compounds have isomers like dextro and levo rotatory forms. Among medicines one isomer is active than other.

Ex:- Levo DopA is used in parkinsonism while dextro isomer is inactive

Dextro amphetamine is active and less active in Levo form.

* Medicinal chemistry analyses the physical properties of the drugs like solubility melting point, etc. Solubility decides how the drug is to be formulated. If it water insoluble, it is converted to some salt form.

Other physical properties like light sensitivity : Crystalline / Amorphous mixtures are also studied. Melting point decides the purity of the compound and how f

the compound is stable at roomtemperature and how it should be handled during medicine formulation. Light sensitivity indicate how the drug has to be preserved.

* Medicinal chemistry also analyses the chemical properties like pH, saturation, internal bonds, helps in different ways. If a compound is acidic, it means it is insoluble in acidic medium in stomach and soluble in basic medium like Intestine. So the pH of the compound helps to design simple tablet or sustained release one so as to release medicine in the intestine.

* Helps in prediction of metabolites of a drug after metabolism.

HISTORY AND DEVELOPMENT OF MEDICINAL CHEMISTRY

- In history, large number of plants were used to treat diseases.
- The 19th century is regarded as the birth period of modern medicinal chemistry with the introduction of side chain theory of drug action in 1885 by Berlin immunologist Ehrlich.
- later in the year 1891, he introduced the term chemotherapy and defined it as " the chemical entities exhibiting selective toxicities against particular infectious agent.
- Large number of Alkaloids like Morphine, Quinine, Atropines were isolated during this century. In the middle of 19th century ideas of chemical structures were generated and first theories of Relationships between chemical structure and biological activity of a drug emerged.
- In the united states, medicinal chemistry was first started as the division of pharmaceutical chemistry (1909-1920), was modified into division of medicinal products (1920-1948) and later got its name the division of medicinal chemistry from the American Chemical Society.

* Research on enzyme specificity (Lock and Key theory) by Fischer in 1894 and Henry's hypothesis on enzyme substrate complex formation in 1903 were regarded as key advancements in the principles of drug design and modern

Further development of medicinal chemistry takes place in the second half of the 20th century. Some of the developments are as follows

Induced fit theory of charge transfer

Concepts of drug latentiation and prodrug

Hansch and others in 1960s given application of mathematical methods to medicinal chemistry and transformation of SAR studies into QSAR.

Application of Artificial intelligence to drug Research

Development of Aspirin

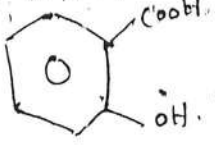
In the year 1763, Edward Woodstone has noticed that chewing of leaves of Salix alba (willow tree) has decreased the symptoms of malaria.

Later in the year 1827, isolation of salicin was done and Biological effects were also being studied. Later in the year 1833, chemical reactions on salicin was initiated.

Salicin was subjected to hydrolysis reaction to form salicyl alcohol and glucose.

Salicyl alcohol was subjected to further oxidation to form salicylic acid.

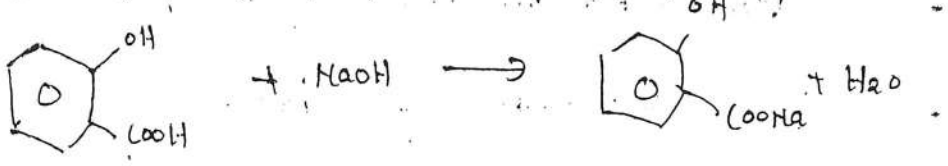
which was done by Raffel Pivia.



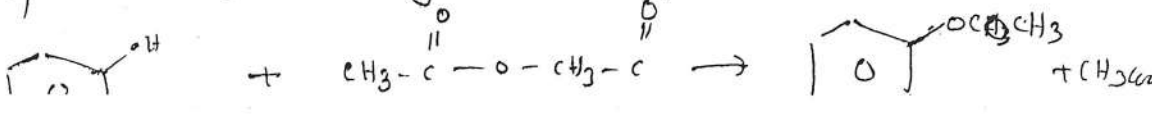
unfortunately salicylic produced some side effects like gastric irritation, formation of ulcers, Burning sensation in mouth, oesophagus etc.

This is mainly due to acidic functionalities in salicylic acid. To reduce the acidity of salicylic acid, it was converted to sodium salicylate. Even though it has produced similar biological effects as that of lead compound it has unpleasant taste.

(Nauseating)



Later Aspirin was synthesised by Acetylation of salicylic acid. (Acetyl Salicylic acid)



3500 BC — Sumerians reported use of opium

1793 — Fauteray and Vauquelin was the first to introduce chemistry into pharmacy curriculum.

1818 — Meissner proposed the term alkaloids.

1820 — Isolation of Morphine, Quinine and Atropine

1842 — onwards general anesthetics were introduced, antiseptics like Iodine and phenol were used.

1853 — Henry proposed the relationship between functional groups and their Biological activity

1875 — Carl buss isolated salicylic acid from spirea ulmaria.

1890 — Hoffmann named Acetyl salicylic acid as aspirin.

1892 — Benzocaine was obtained by structural modification of cocaine.

1899-1901 — Meyer and overton related partition coefficient with Biological activity.

1911 — Barbiturates were introduced as sedative.

1930 — structure of steroid hormone

1926-1946 — Synthetic antimalarials like chloroquine were introduced as substitute / Quinine

1944-1949 — Isolation of Antibiotics — streptomycin, chloramphenicol & tetracycline

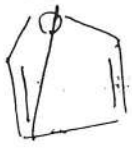
1950-1960 — Semisynthetic Corticosteroids — prednisolone, Betamethasone were prepared.

1889 — Aspirin was introduced by Dresser

1778-1829 — Davy introduced nitrous oxide (laughing gas) as inhalation anesthetic.

1903 — Barbital was innovated by emil Fischer & Mering

1904 — Stolz synthesized first hormone epinephrine



PHYSICO CHEMICAL PROPERTIES IN RELATION TO BIOLOGICAL ACTION.

— The ability of a chemical compound to elicit a pharmacological / therapeutic effect is related to the influence of various physicochemical properties of the chemical substance ('Drug') on the biomolecule (Receptor) that interacts with.

→ physical property of drug is responsible for its action.

→ chemical properties — The drug react extracellularly according to simple chemical reactions like neutralisation, chelation, oxidation etc.

— Various physico-chemical properties are.

1. Solubility
2. partition coefficient
3. Ionization
4. chelation
5. Hydrogen bonding
6. protein Binding
7. Bioisosterism
8. optical and Geometrical Isomerism.

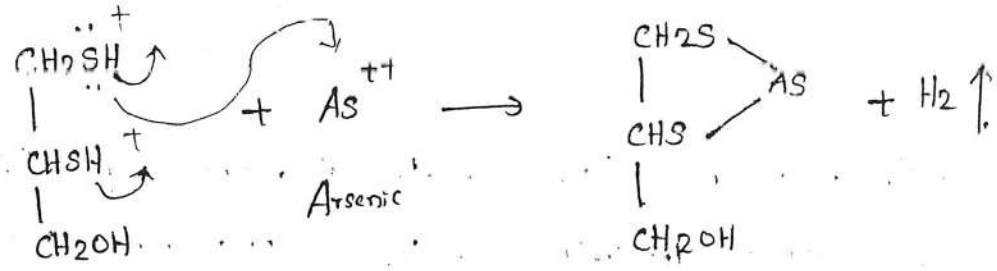
CHELATION / complexation

The compounds that are obtained by donating electrons to a metal ion with the formation of ring structure are called chelates and the phenomena is known as chelation / complexation.

Ligands :- The compounds capable of forming a ring structure with metal is termed as ligands.

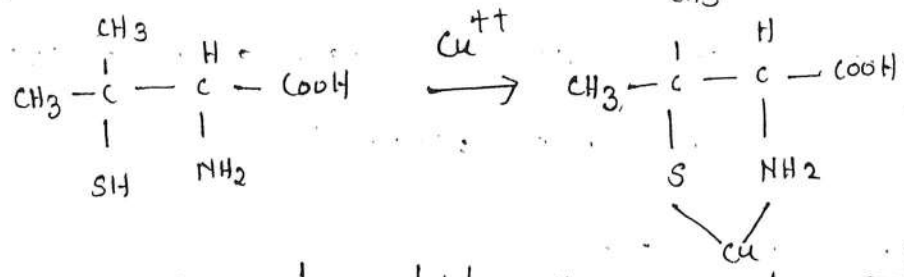
Importance of chelates in medicine

1. Dimercaprol is a chelating agent used in the treatment of Arsenic poisoning

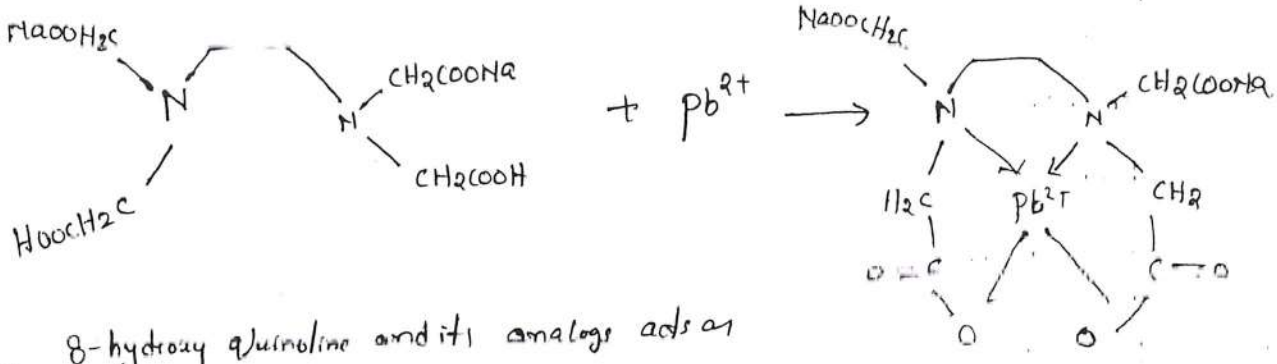


Dimercaprol. chelate.

2. Penicillamine → used in Wilsons disease – where there is excess of Cu^{++} in the body.
   → used in copper poisoning and Arsenic poisoning as second line drug.

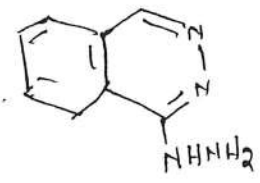


3. Disodium EDTA forms chelates with various toxic metal ions and helps in their excretion. Ex:- lead poisoning.



6. 8-hydroxy quinoline and its analogs acts as antibacterial & fungal agent by complexing with Iron & copper. excreted in urine ← water soluble ← lead-EDTA Chelate.

4. A side effect of Hydralazine, a antihypertensive agent is formation of anemia and this is due to chelation of the drug with Iron.



+ Iron (Haemoglobin) → Hydralazine - Iron complex.

5. Dimethyl amino group and enolic group present in tetracycline antibiotics easily forms chelates with Ca^{2+}, Mg^{2+}, Al^{3+} ions. Because this absorption is decreased and delayed, when tetracyclines are taken with milk or antacids and iron/zinc salts

HYDROGEN BONDING

* Hydrogen bonding is relatively weak bonding which exists between Hydrogen atom and electronegative atoms like F, Cl, N, O, & S. denoted by dotted lines.

* The compounds that are capable of forming hydrogen bonding is only soluble in water.

Classification :-

1. Intermolecular hydrogen bonding — when the hydrogen bond is present between two atoms of two different molecules, then it is known as intermolecular hydrogen bond.

BIOISOSTERISM

* Certain drugs and chemical substituents or functional groups have same physical or chemical properties and produces similar biological properties are known as bioisosteres and the relation between bioisosteres is known as Bioisosterism.

* The concept of bioisosterism comes from isosterism and Isosteres introduced by "Longmuir". According to him, isosteres are the compounds having same number of electrons and arrangement of $\bar{e}$ is also similar. Due to the presence of same number of electrons, these functional groups have similar physical and chemical properties. Such isosteres when produces similar biological properties are known as Bioisosteres.

Importance in Drug design

1. In order to increase the required biological or physical properties of the drug, without changing its chemical scaffold, bioisosterism is required.
2. It is also used to Reduce toxicity, alter the activity, or to change the Bioavailability of the drug molecule.

Classification of Bioisosteres — They are broadly classified into

1. Classical Bioisosteres
2. Non-classical Bioisosteres.

Classical Bioisosteres — They have similarities of shape and electronic configuration of atoms, groups and molecules which they replace.

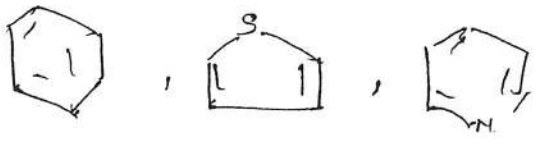
— These are further classified as

i) Univalent atoms — $-Cl$, $-SH$, $-OH$, $-CH_3$, $-NH_2$

ii) Bivalent atoms — $-O$, $-S$, $CONH$, COO, $-COCH_3$

iii) Trivalent atoms — $-CH=$, $-N=$

iv) Tetravalent atoms — $=C=$, $=P^{+}=$, $=\overset{+}{N}=$

v) Ring equivalents :— 

Optical Isomerism

Stereochemistry of the drug molecule greatly affects the action of the drug as it alters the interaction of the drug with a Receptor, The main biological activity is present only in one of the stereoisomers.

— Optical Isomerism arises due to difference in rotation of plane polarised light by the drug molecule ie drug may be (+) dextrorotatory (or) (−) levorotatory.

Ex:- a) (−) adrenaline is more active than (+) Adrenaline

b) (−) warfarin is 5 times more potent than (+) isomer

c) (−) propronolol is more than potent than (+) propronolol.

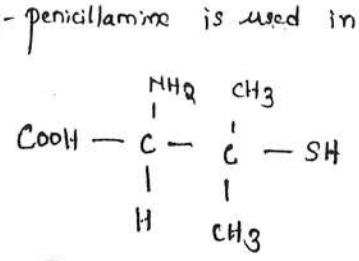
d) (+) Amphetamine is 3-4- times more active than (−) isomer

e) L- thyroxine has thyroid activity and D- thyroxine has antihypercholesterolemic activity.

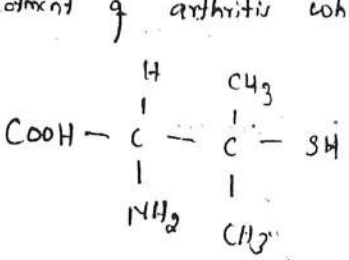
— Stereospecificity of a particular isomer depends on interaction of the drug with its Receptor. There should be 3 point attachment with the receptor if there is only 2-point attachment of drug molecule with Receptor, then there will be no biological activity.

* In certain cases, one isomer is active while the other isomer is toxic

Ex:- D- penicillamine is used in the treatment of arthritis while L- penicillamine is toxic



D- penicillamine

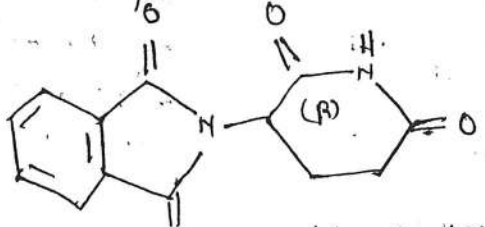


L- penicillamine.

* Many enantiomers have different taste and odour

Ex: D- Asparginine — Sweet taste L- Asparoginine — Tasteless

*



Thalidomide (R)

— Treatment of morning sickness in Pregnant women — Sedative effect

S-isomer of Thalidomide has birth defects / teratogenic effects

→ Shortened arms and hands and not functional.

→ Drug harms the foetus or worn

Non-classical Bioisosteres

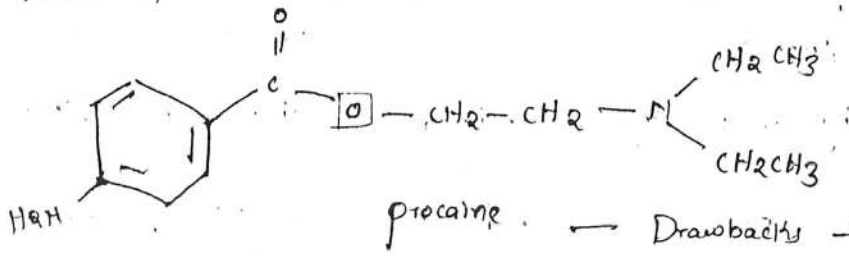
— These molecules do not follow steric and electronic rules of classical bioisosteres but they have similar biological properties.

Ex:- $-Cl$, $-CF_3$, $-C\equiv N$

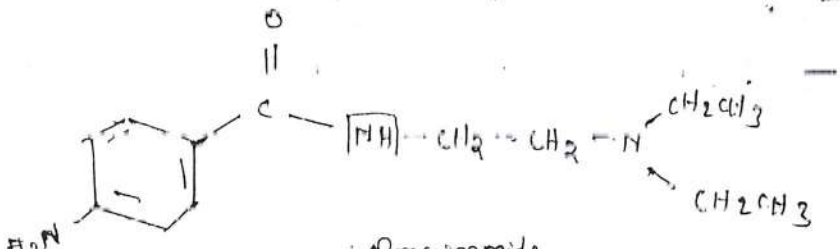
ii) 

Pharmaceutical Applications of Bioisosterism

1. Procainamide has long duration of action than procaine, this involves isosteric placement of oxygen with a Nitrogen atom.



procaine — Drawbacks — orally inactive drug
— short duration of action

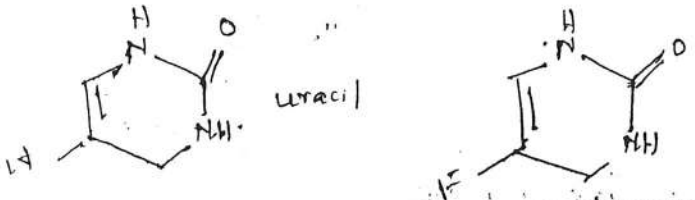


procainamide

— Amides are resistant to enzymatic and chemical hydrolysis

2. Substitution of H-atom of uracil by 'F' atom gives 5-Fluorouracil

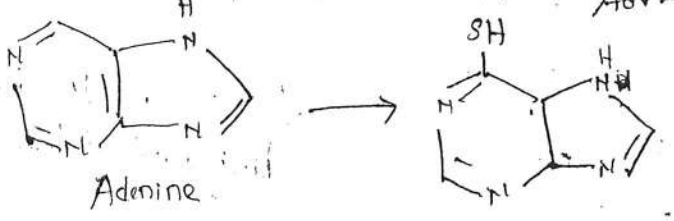
— Long duration of action
— Antiarrhythmic drug with mild local anesthetic action



uracil

5-Fluorouracil — Anticancer drug.

Adv → Lipophilicity has increased with fluorine. So the drug has faster penetration into Biological membrane and shows good activity.

3. 

Adenine

Mercaptopurine

PROTEIN BINDING

* It Refers to the degree to which drugs attach to proteins within the Blood.

— Common Blood proteins that bind are Human serum Albumin (HSA), α, β, γ globulins, lipoproteins, glycoproteins.

* Depending upon the drugs specific affinity for plasma protein, they exists in two form

1. Bound form — These drugs cannot diffuse through the capillary wall to reach site of action (inactive)
2. unbound form (or) free form — Exhibits pharmacological / Biological effect. also it is the fraction that may be metabolised or excreted ← active form the drug.

Significance of protein / tissue binding of drug:

a. Absorption — When there is more protein binding, then it disturbs the absorption equilibrium.

b. Distribution — A protein bound drug in particular does not cross BBB, placental barrier and the glomerulus. Thus protein binding decreases the distribute of drug.

c. Metabolism — protein binding decreases the metabolism of drugs and enhance the Biological half life. only unbound fraction gets metabolised

e.g: phenyl butazone & sulfonamide.

d. Elimination — only the unbound form of drug is capable of elimination.

— protein binding prevent the entry of drug to the metabolising organ (liver) and to glomerular filtration. e.g Tetracycline is eliminated by glomerular filtration

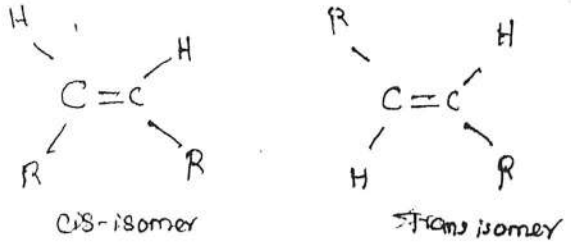
e) Drug action — protein binding inactivates the drugs because sufficient concentration of drug cannot be build up in the Receptor site for action

f. Sustained Release — The complex of drug protein in the blood act as a Reservoir and continously supply the free drug.

g. Diagnosis — The chlorine atom of chloroquine replaced with radiolabelled I-131 can be used to visualise melanomas of eye and disorders of thyroid gland.

Geometrical Isomerism

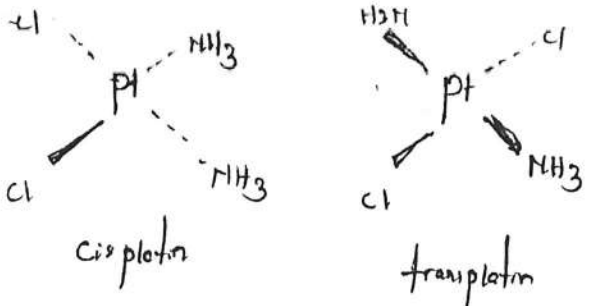
It occurs as a result of or due to the presence of carbon-carbon double bond (C=C). This isomerism is represented by cis and trans isomerism. This arrangement of atoms around C=C Bond greatly affect the biological activity.



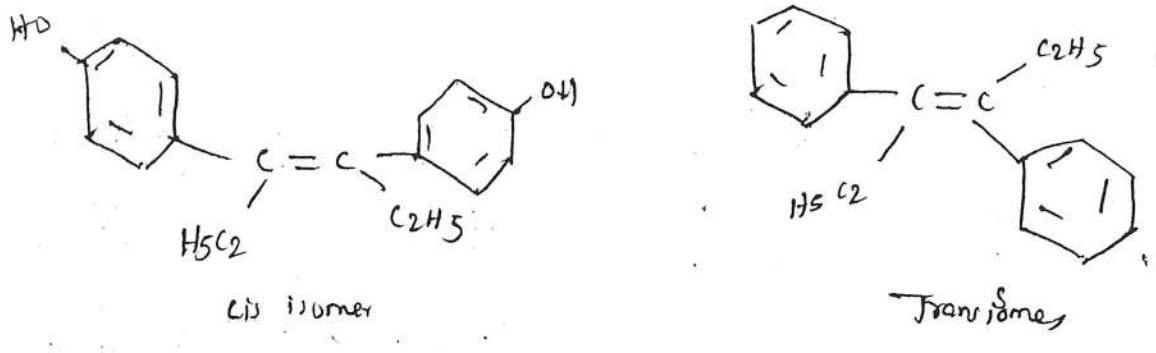
Whether a molecule is a cis-isomer or trans-isomer it can create different pharmacological activities.

Ex:- Consider the isomers of diammine dichloroplatinum (Cisplatin - Antineoplastic drug)

Cisplatin is highly effective in treating testicular and ovarian cancers while transplatin. Since inside the nucleus, only the cis isomer has the correct orientation to bind the cancer cell's DNA.



Trans-diethyl stilbestrol is more potent than cis isomer. ie it has higher estrogenic activity



PARTITION – COEFFICIENT

The lipophilicity of an organic compound is usually described in terms of partion Coefficient, log p which can be defined as the ratio of concentration of drug molecule in lipid phase and water phase.

$$\log p = \frac{\text{Concentration of drug in lipid/organic phase}}{\text{concentration of drug in water phase.}}$$

- partition coefficient determines the transport and diffusion of the drug across the cell membrane. Generally compounds with log p values between 3 and 6 shows good absorption, where as log p greater than 6 and less than 3 have poor transport characteristics.

Methods to determine log p

- 1. Shake flask method — experimentally, log p can calculated by shaking a known amount of drug with octanol and water layers and then calculate the amount of drug both phase ie organic and aqueous phase.

Other methods — HPLC Method, Membrane partition method etc, electrochemical method, slow-stirring method

* The partition coefficient value (π) expresses the relative free energy change occuring when a drug molecule moves from one phase to another.

  +ve π value — drug favours organic phase

  −ve π value — " " Aqueous "

* log p values in the range of 1.5 - 3.0 serve as a passport for the easy entry into the brain, where these drugs may produce sedative effects.

* Lipophilicity governs the CNS penetration of a drug. Certain drugs disturb the brain function and may exhibit lethal effect. Toxicity of such agents was found to mainly governed by their lipophilic character. Therefore log p is a parameter of major importance in drug development.

Solubility — It is the analytical composition of a saturated solution expressed as a proportion of designated solute in designated solvent.

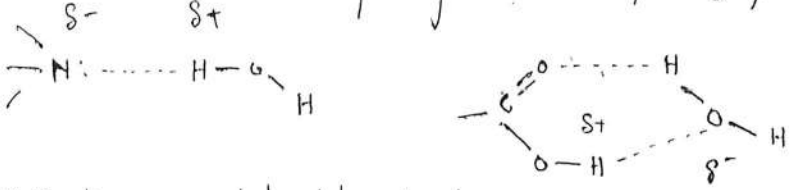
Importance — 1 Formulation of the drug in an Appropriate dosage forms.

2. Bio-disposition - Disposition of organic medicinal agents in the living system after administration (ADME)

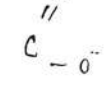
- In order for a chemical compound to dissolve in a particular solvent / medium, the compound must establish attractive forces between itself and molecules of the solvent. The most important intermolecular attractive forces (bonds) that are involved in the solubilization process are:

1 Vandervaals Attraction — Weakest intermolecular force (0.5 – 1.0 Kcal/mole)
- Occurs between non polar groups (hydrocarbons)
- Temperature Dependent.

2 Dipole - Dipole Bonding — stronger (1.0 – 10 Kcal/mole)
- occurs electrostatically between electron deficient and electron rich atoms
- hydrogen bonding is a specific example of this bonding and serves as primary contributer for hydrophilicity.

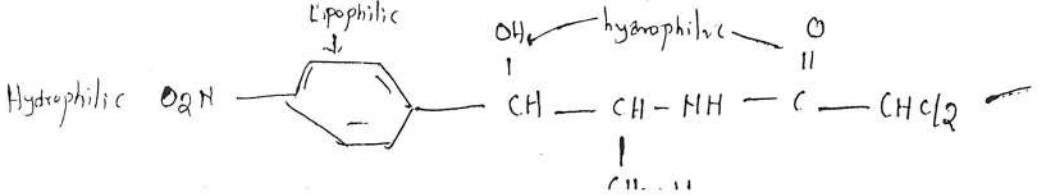


3 Ionic Bonding — electrostatic attraction between cations and Anions. Common in Inorganic compounds and salts of organic compounds.



4. Ion - Dipole bonding — electrostatic interaction between cation / anion.
- Relatively strong (1-5 K.cal/mol)
- important attraction between organic medicinal agent & water.

* The Relative solubility of an organic medicinal agent is a function of the presence of both lipophilic and hydrophilic features within its structure which serves to determine the extent of interaction of DMA with lipid / aqueous phase.

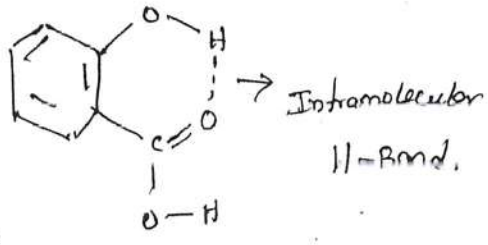


Method 2:-

$$\% \text{ Ionised} = \frac{100}{1 + 10^{PKa - PH}}$$

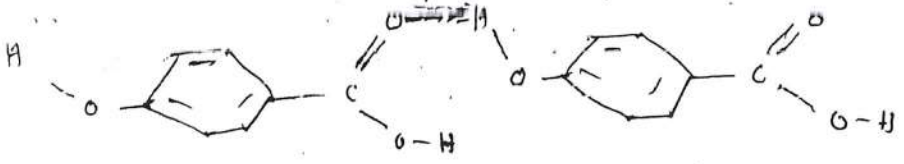
$$= \frac{100}{1 + 10^{7-7.4}} = \frac{100}{1 + 10^{0.4}} = \frac{100}{1 + 2.51} = \frac{100}{3.51} =$$

Ex2:- Salicylic acid (o-hydroxy benzoic acid) has appreciable antibacterial activity, but the para isomer (p-hydroxy benzoic acid) is inactive, because salicylic acid (ortho isomer) can form intramolecular hydrogen-bonds,



→ Intramolecular H-Bond.

M and p-isomers of salicylic acid can form only inter-molecular H-Bond.



p-hydroxy Benzoic acid (dimer).

→ Salicylic acid has less solubility in water than the p-isomer but its log P is 300 times more, while p-hydroxy benzoic acid has low log P value and hence low antibacterial action.

Hydrogen Bonding

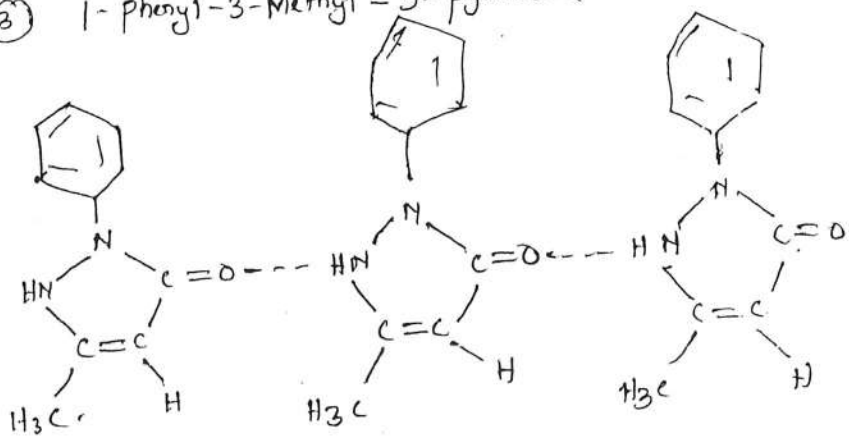
- It is relatively weak bonding which exist between hydrogen atom and electronegative atoms like F, Cl, N, O, S and denoted by dotted lines.
- The compounds that are capable of forming hydrogen bonding is only soluble in water.

↑ occur between two neighbouring molecule.

Intermolecular hydrogen bonding — when the hydrogen bond is present between two atoms of.

Intramolecular hydrogen bonding — occur within the molecule.

Ex:- (3) 1-Phenyl-3-Methyl-5-pyrazolone ← shows no analgesic properties.

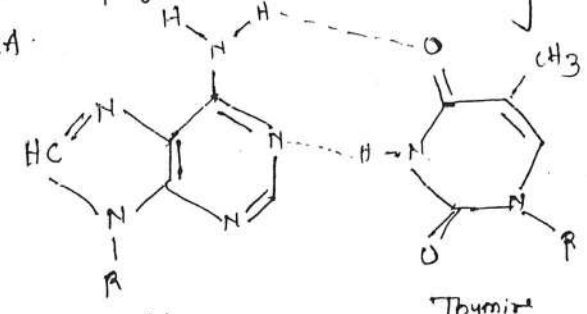


Antipyrine cannot form H-Bonds due to weak attraction force hence it is freely soluble in Non-polar solvents and has proper log P value to penetrate the CNS

Antipyrine (1-phenyl, 2,3-dimethyl-5-pyrazolone)

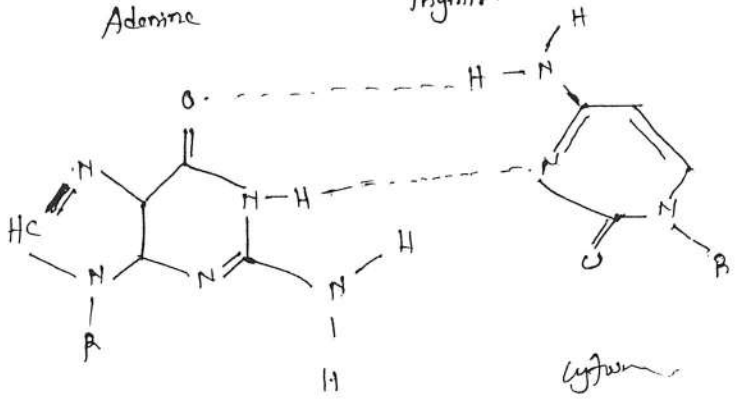
Importance

(1) H-Bonds play a key role in maintaining the structural Integrity of the base pairs of DNA.



Adenine

Thymine



Guanine

Cytosine

Applications of Solubility

- Solubility of a substance serves as a standard test for purity.
- The action of a drug can be severely limited by poor aqueous solubility. Similarly, side effects of certain drugs are the result of their poor aqueous solubility.
- The solubility of drugs in GI fluids is an important step for better absorption of drugs.
- Solubility is said to be one of the characteristic properties of a substance, to indicate a substance polarity, to help to distinguish it from other substances and also a guide to application of the substance.
- Solubility of a substance is useful when separating mixtures.
  Ex: mixture of salt (NaCl) and silica may be separated by dissolving the salt in water and filtering off the undissolved silica.

IONIZATION

- Ionized form imparts good water solubility to the drug which is essential for good binding interactions of drug with its receptor.
  While non-ionised form helps the drug to cross cell membranes. Hence, good balance of Ionized : non-ionised forms is essential for better pharmacokinetic and pharmacodynamic features.
- Most of the drugs having pKa value in the range of 6-8. Hence they are partially ionised at Blood pH to create balanced ratio of ionised : non ionised form.
- The Rate of absorption of a drug which is capable of existing both in ionised and unionised forms, is dependent on the concentration of unionised form rather than its total concentration. The unionised form of a drug is dependent on two factors i) pKa ii) pH of the environment
- It is Represented by Henderson - Hasselbach equation

For acid, $pKa - pH = \log (C_u / C_i)$

For Base, $pKa - pH = \log (C_i / C_u)$

Where C_i and C_u are the concentrations of ionised and unionised drugs respectively.

Ex % Ionised calculations of Drug × pKa 7. calculate % ionised in Blood (pH 7.4) and urine (pH 6.2)

$\log_{10} x = y \Rightarrow \boxed{x = 10^y}$

$pH = pKa + \log_{10} \left(\frac{I}{U} \right)$ ← salt / acid.

$pH - pKa = \log_{10} \left(\frac{I}{U} \right) \rightarrow 10^{pH - pKa} = \left(\frac{I}{U} \right)$ — eqv. (1)

eqv. 2 $\%I = \frac{I}{U + I} \times 100$

Rewrite the eqv. (2) $\frac{\frac{I}{U}}{\frac{I}{U} + 1} \times 100$ — eqv. (3)

$10^{pH - pKa} \rightarrow 10^{7.4 - 7} = 10^{0.4} \Rightarrow 2.51$

$\Rightarrow \frac{2.51}{2.51 + 1} \times 100 = 71.5$

URINE $10^{pH - pKa} = \frac{I}{U}$

$10^{6.2 - 7} = 10^{-0.8} = 0.16 \Rightarrow \frac{\frac{I}{U}}{\frac{I}{U} + 1}$

Method 2:-

$\%$ Ionised $= \frac{100}{1 + 10^{pKa - pH}}$

$= \frac{0.16}{0.16 + 1} \times 100 = 13.7$

Drug Metabolism / Biotransformation / Detoxification.

Definition — Series of Biochemical reactions occuring in the body to convert toxic / non-polar / lipid soluble compounds to nontoxic / polar / water soluble and more excretable forms.

Site of detoxification — Liver, partially in Kidneys.

Mechanism of Detoxification

phase I reactions — Oxidation, Reduction, Hydrolysis.

phase II Reactions — Conjugation Reactions

Oxidation — large number of foreign substances are detoxified by oxidation

ex- Alcohols, Aldehydes, Amines, Aromatic Co. hydrocarbons and sulfur compounds

Alcohols — Aliphatic and Aromatic Alcohols undergo oxidation to form Corresponding acids

i) $CH_3OH \rightarrow HCOOH$
Methanol — formic acid

ii) $C_2H_5OH \longrightarrow CH_3COOH$
ethanol — Acetic acid

iii) $C_6H_5CH_2OH \longrightarrow C_6H_5COOH$
Benzyl alcohol — Benzoic acid

ii) Aldehydes → Aldehydes are oxidised to produce corresponding acids.

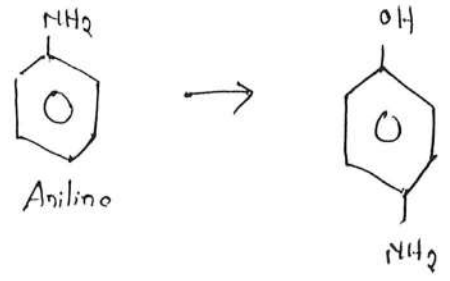
$C_6H_5CHO \longrightarrow C_6H_5COOH$
Benzaldehyde — Benzoic acid

Amines and their derivatives

Aliphatic amines are converted to acids, liberating urea while aromatic amines are oxidised to phenols.

$RCH_2NH_2 \longrightarrow R-COOH + NH_2-CO-NH_2$

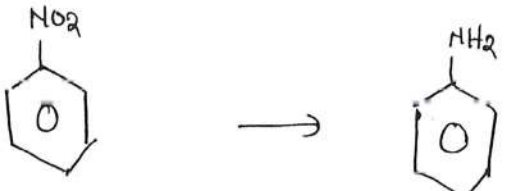
Aliphatic amine. Aliphatic acid urea



Aniline p-amino phenol

Reduction

i)



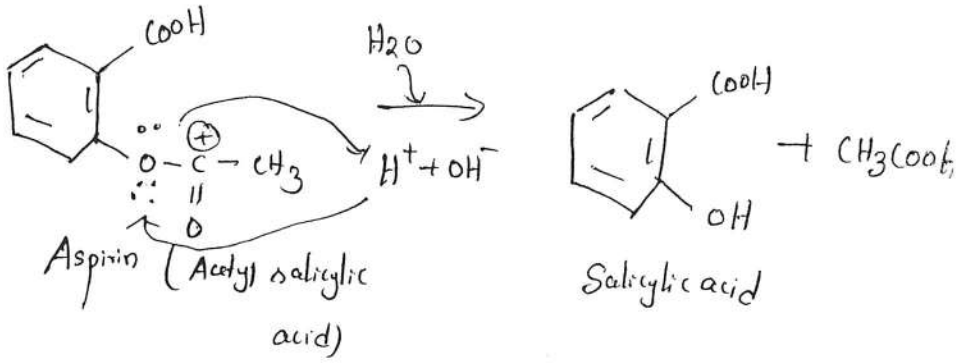
Nitro benzene Aniline

ii) $C_6H_2OH(NO_2)_3 \longrightarrow C_6H_2OH(NO_2)_2NH_2$

picric acid. picramic acid

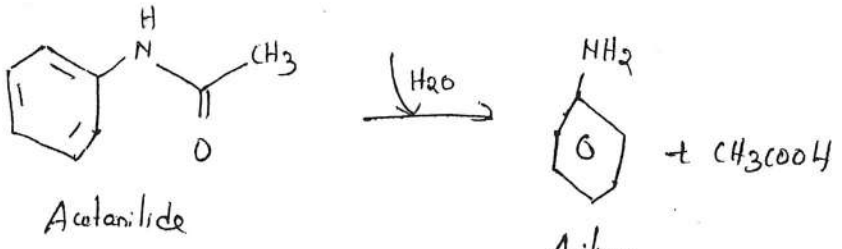
iii) HYDROLYSIS

Examples



Aspirin (Acetyl salicylic acid) Salicylic acid

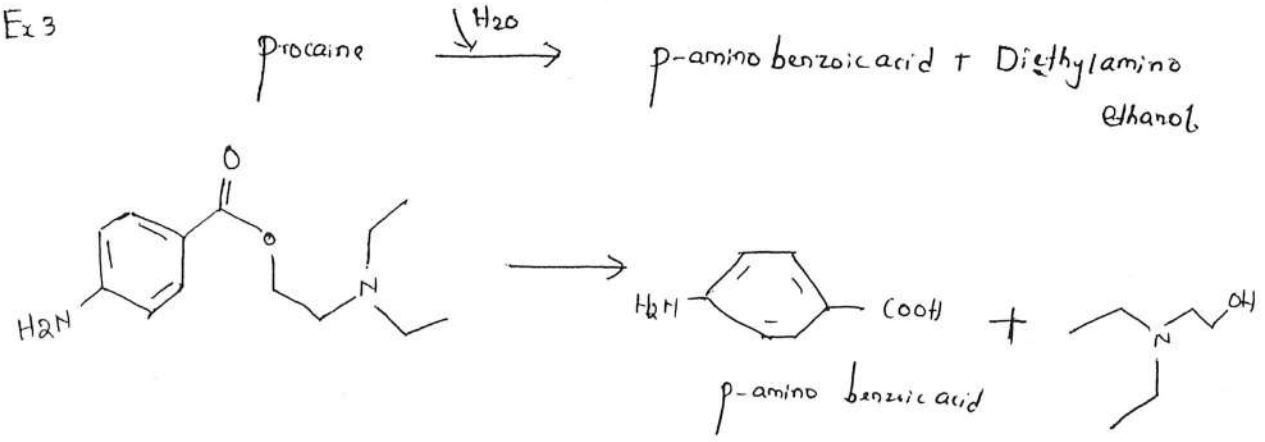
Ex 2



Acetanilide

Anilino

Ex 3



p-amino benzoic acid

diethylamino ethanol

CONJUGATION REACTIONS

(PHASE-II REACTIONS)

Conjugation is the process of in which a foreign compound combines with a substance produced in the body.

Several drugs undergo detoxification by conjugation to produce less toxic and more excretable forms.

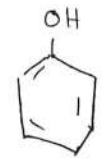
Conjugating substances — Glucuronic acid
glycine
glutamine
methyl group
Acetic acid, thiosulfate
cysteine (of glutathione)

Glucuronic acid — Active form of glucuronic acid is *UDP-glucuronic acid*

— Microsomal enzymes i.e glucuronyl transferase participate in glucuronide conjugation.

$$X-\overset{-}{O}-\overset{+}{H} + \text{UDP-glucuronic acid} \xrightarrow[\text{transferase}]{\text{UDP-glucuronyl}} X\text{O-glucuronide} + \text{UDP}$$

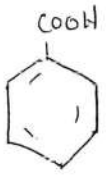
— Glucuronic acid conjugation may occur with compounds containing —OH, carbonyl, —SH / NH_2 groups.



phenol + UDP-glucuronic acid ⟶

+ UDP

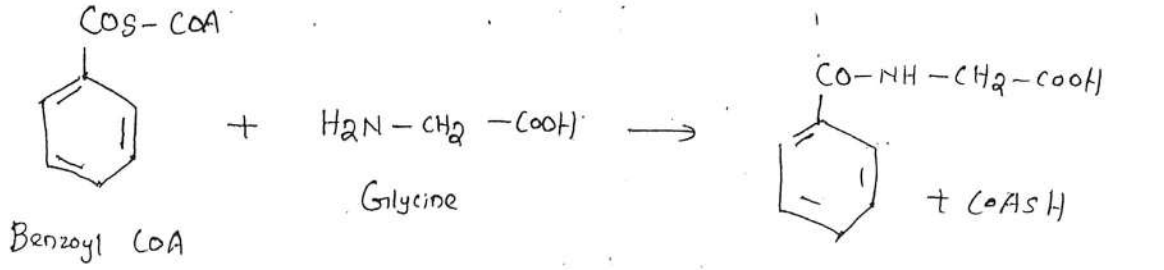
phenyl glucuronide.



Benzoic acid + UDP-glucuronic acid ⟶ Benzoyl glucuronide + UDP.

GLUTATHIONE (Glu-cys-gly) — active conjugating agent.

— Organic compounds such as Alkyl halides, Alkenes, Nitro compounds, & epoxides. get conjugated with cysteine of glutathione. to form mercapturic acid. The glutamate and glycine of glutathione are removed and acetyl group is added to cysteine residue.



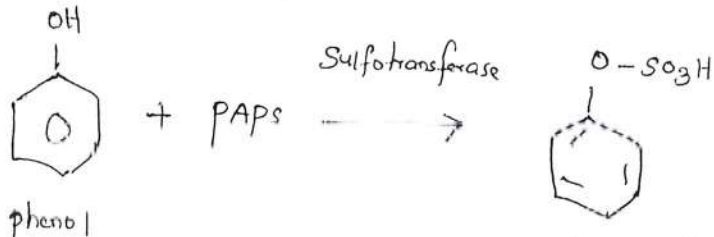
Benzoyl CoA

Hippuric acid (Benzoylglycine)

SULFATE CONJUGATION

Active form of sulfate conjugation – 3'-phosphoadenosine-5-phosphosulfate (PAPS).

participates in conjugation reactions and the enzyme sulfotransferase is involved



phenol

phenyl sulfate

phosphoadenosyl phosphate

ACETIC ACID

– Acetyl CoA is the active form of Acetic acid that takes part in conjugating reactions.

Ex:- Sulfanilamide + Acetyl CoA → Acetylsulfanilamide + CoASH

Thiosulfate – Highly toxic cyanides are conjugated with thiosulfates to form less toxic thiocyanate.

Cyanide + sodium thiosulfate → Thiocyanate + sodium sulfate.

(Drug) ← $R-X$ + GSH (Glutathione) – tripeptide

HX ← GSH transferase

$R-SG$

Glutamate ← γ-glutamyl transpeptidase

Cysteinyl glycine

Glycine ← Cysteinyl glycinase

$R-S-CH_2-CH(NH_2)-COOH$

R-cysteine.

Acetyl CoA → N-Acetyl transferase ← CoASH

$R-S-CH_2-CH(NH-COCH_3)-COOH$

Mercapturic acid

ROLE OF GLUTATHIONE IN CONJUGATION TO FORM MERCAPTURIC ACID

GLYCINE CONJUGATION:

- Many Aromatic carboxylic acids (Benzoic acid, phenyl acetic acid) are conjugated with glycine.
- Hippuric acid is formed when glycine is conjugated with benzyl CoA.

Example – oral contraceptive steroids $\xrightarrow[\uparrow \text{induction}]{\text{CYP3A4}}$ Inactive, excreted.

Rifampin

b) Enzyme Inhibition

– A decrease in drug metabolising activity of an enzyme is called as enzyme inhibitio

– The process of inhibition may be direct or indirect.

1. Direct Inhibition – It may result from interaction at enzymatic site. The net outcome being a change in enzyme activity.

– Direct enzyme Inhibition can occur by one of the following mechanisms.

i) Competitive Inhibition – occurs when structurally similar compounds compete with for the same site on an enzyme.

ii) Non-competitive inhibition – occurs when structurally unrelated agent interact with th enzyme and prevents the metabolism of drug

iii) Product inhibition – occurs when metabolic product competes with the substrate for the same enzyme

2. Indirect Inhibition – It is caused by one of the following mechanism

i) Repression – It may be due to fall in the rate of enzyme synthesis or rise in the rate of enzyme degradation.

iv) Altered physiology – It may be due to Nutritional deficiency or hormonal imbalance

Factors Affecting Drug metabolism

A Number of factors may influence the metabolic rate of a drug

1. Chemical factors
   a) enzyme Induction
   b) enzyme Inhibition
   c) environmental chemicals
2. Biological factors
   a) Age
   b) Diet
   c) Sex difference
   d) species difference
   e) strain difference
   f) Altered physiological factors.
3. physicochemical properties of the drug.
4. Stereochemical aspects of the drugs

Stereochemical aspects — Stereochemistry also affects the metabolism of drugs.

— Stereoselective metabolism of drugs - Metabolising enzymes have different preference for one enantiomers than the other hence result in enantioselectivity.

Ex: (-) quinine treats malaria fever but (+) quinine does not

D(+) glucose gets metabolized in the body to give CO_2 & H_2O but L-(-) glucose is not metabolized

CHEMICAL FACTORS

a) Enzyme Induction

The phenomena of increased drug metabolising ability of enzymes by several drugs and chemicals is called as enzyme Induction and the agents which bring about such an effect are called enzyme Inducers.

Consequences of enzyme Induction

— Decrease in pharmacological activity of drugs
— Increased activity where the metabolites are active
— Altered physiological status due to enhanced metabolism of endogenous compounds

b) DIET :- The enzyme content and activity is changed by number of dietary components.

* Low protein diet decreases and high protein diet increases the drug metabolising ability as enzyme synthesis is promoted by protein diet and also raises the level of amino acids for conjugation with drugs.

* Fat free diet decreases cytochrome-p-450 levels since phospholipids, which are important components of microsomes become deficient.

* Dietary deficiency of vitamins like Vitamin A, B_2, B_3, C and E and minerals such as Fe, Ca, Mg, Zn retard the metabolic activity of enzymes.

* Starvation results in decreased amount of glucuronides formed than under normal conditions.

c) Sex difference

Sex related differences in the rate of metabolism may be due to sex hormones. Such sex differences are widely studied in rats where male rats have greater drug metabolising capacity.

— In humans, women metabolise benzodiazepines slowly than men.

d) Species difference

Species difference have been observed in both phase-I and phase II reactions.

— In phase I reactions, both qualitative and quantitative variations in the enzyme and their activity have been observed.

— Qualitative differences among species generally result from the presence or absence of specific enzymes in the species.

c) Environmental chemicals

Several environmental agents influence the drug metabolising ability of enzymes.

Ex:- i) organophosphate insecticides & heavy metals such as mercury, cobalt, nickel, Arsenic inhibit drug metabolising ability of enzymes.

ii) Halogenated pesticides such as DDT, polycyclic aromatic hydrocarbons contained in cigarette smoke have enzyme induction effect

iii) others factors that may influence drug metabolism are temperature, altitude, pressure, atmosphere etc.

BIOLOGICAL FACTORS

- The drug metabolic rate in different age groups differs mainly due to variations in
1) AGE the enzyme content, enzyme activity and haemodynamics.

* In neonates (upto months (two) and in infants (2 months to 1 year), the microsomal enzyme system is not fully developed. So, many drugs are metabolised slowly.
e.g:- Caffeine has a t/2 of 4 days in neonates in comparision to 4 hrs in adult

* Children (between 1 year & 12 years) metabolise several drugs much more rapidly than adults as the rate of metabolism reaches a maximum somewhere between 6 months and 12 years. It's a result they require large mg/kg dose in comparision to adult

* In elderly persons (Adult), the liver size is reduced, microsomes enzyme activity is lesser and hepatic blood flow also decreases as a result of reduced cardiac output all of which contributes to decreased metabolism of drugs.

For example – ↑sed concentration of various hormones such as estrogen, progesteron placental growth hormones & prolactin.

– In women, metabolism of promazine and pethidine is reduced during pregnancy

ii) Disease States

There are many disease states that affect metabolism of drugs. Some of them are Cirrhosis of liver, alcoholic liver disease, diabetes mellitus, malaria, Bacterial & Viral infections, Acromegaly etc. It can be be seen that major affect are seen in the

– The possible can disease affecting liver as liver is quantitatively the important site for metabolism. The possible cause in the effect of metabolism due to diseases may be:

* Decreased enzyme activity in liver
* Altered hepatic blood flow
* Hypoalbuminaemia (leading to lower plasma binding of drugs)

iii) Hormonal Imbalance

– Higher level of one hormone may inhibit the activity of few enzymes
– Adrenolectomy, thyroidectomy and alloxan-induced diabetes in animals showed impairment in the enzyme activity with subsequent fall in rate of metabolism.

3. physicochemical Properties of the drug

Molecular size and shape, pKa, acidity / basicity, lipophilicity and steric, electronic characteristics of the drug influence in interaction with active sites of enzy

Importance of drug metabolism: – The therapeutic efficacy, toxicity and biological half-life of a drug depends on the metabolism of the drug and number of factors that affect metabolism of a drug.

— Quantitative differences result from variations in the amount of and localisation of enzymes, the amount of natural inhibitors, and the competition of enzymes for specific substrates.

— Human liver contains less cytochrome-p 450 per gram of tissue than do the livers of other species. For example, rat liver contains approximately 30-50 nmol/g of cytochrome p-450, whereas human liver contains 10 to 20 nmol/g; Furthermore, human liver is 2% of body weight whereas rat liver is 4%.

e) STRAIN DIFFERENCE

Just as the difference in drug metabolising ability between different species is attributed to genetics, the differences are observed between strains of same species also.

Pharmacogenetics — A study of inter-subject variability in drug response is called pharmacogenetics. The inter-subject variation in metabolism may either be monogenetically or polygenetically controlled.

— polygenetic control is observed in twins.

Ethnic Variations — Differences observed in the metabolism of drug among different races are called ethnic variations. Such variation may be monomorphic or polymorphic.

f) Altered physiological factors

i) Pregnancy — It is known to affect hepatic drug metabolism.

— physiological changes during pregnancy are responsible for reported alterations in drug metabolism

Introduction To Autonomous Nervous System.

UNIT-II

* Autonomous Nervous system controls all involuntary actions.
- Provides a homeostasis for the regulation of all metabolic activities/changes in body.
- ANS consists of two main divisions

1. Sympathetic Nervous System
2. parasympathetic Nervous system.

Both these Nervous systems have opposite actions. The sympathetic nervous system has catabolic effects like increase in B.P, contraction of arteries, Relaxation of Bronchial muscles etc.

- The parasympathetic Nervous system has anabolic effects like Contraction of pupils, decrease in B.P, ↑se in activity of the digestive system and GIT secretions.

Neurotransmitters of Adrenergic system

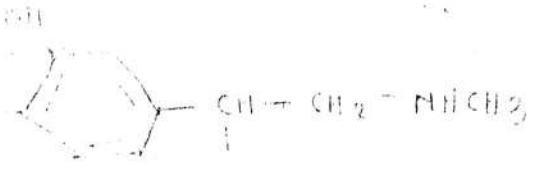
- Belongs to a class Catecholamines. It has a catechol ring (o-dihydroxy benzene) attached to an amino ethyl side chain.

Ex:- Epinephrine, Norepinephrine, Dopamine.

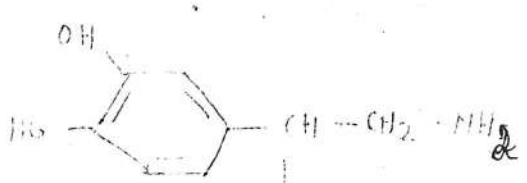
These Neurotransmitters are specific chemical agents which are responsible for transmission of nerve impulse across most of the synapse.

- They are released only when the Nerve impulse produces the response of smooth, cardiac and skeletal muscles, exocrine glands and post synaptic neurons.

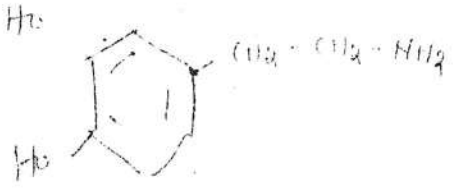
It crosses the synapse and initiates the activity in the another neuron by interaction with the post synaptic receptors.



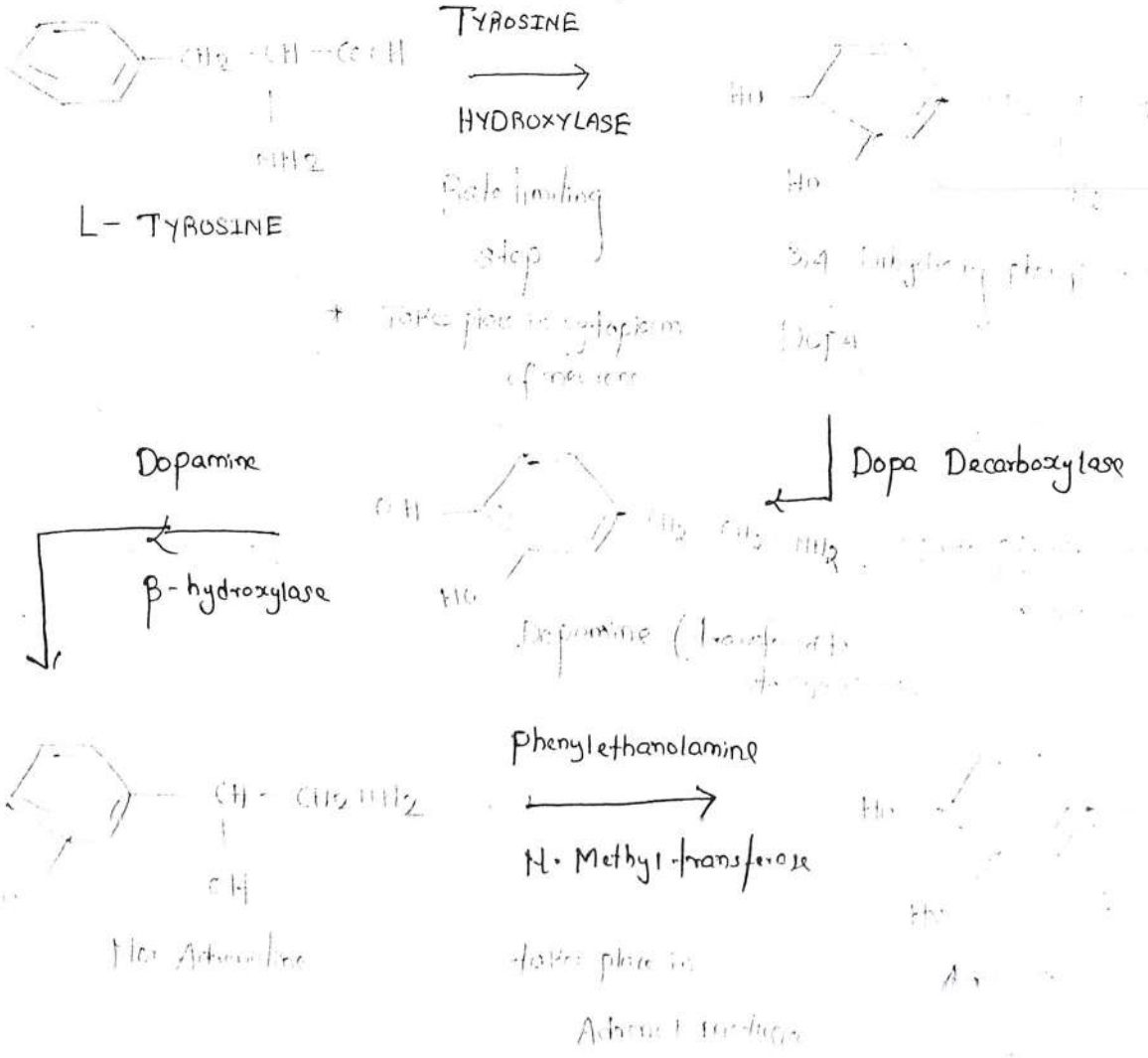
Epinephrine



Norepinephrine



UNIT-II

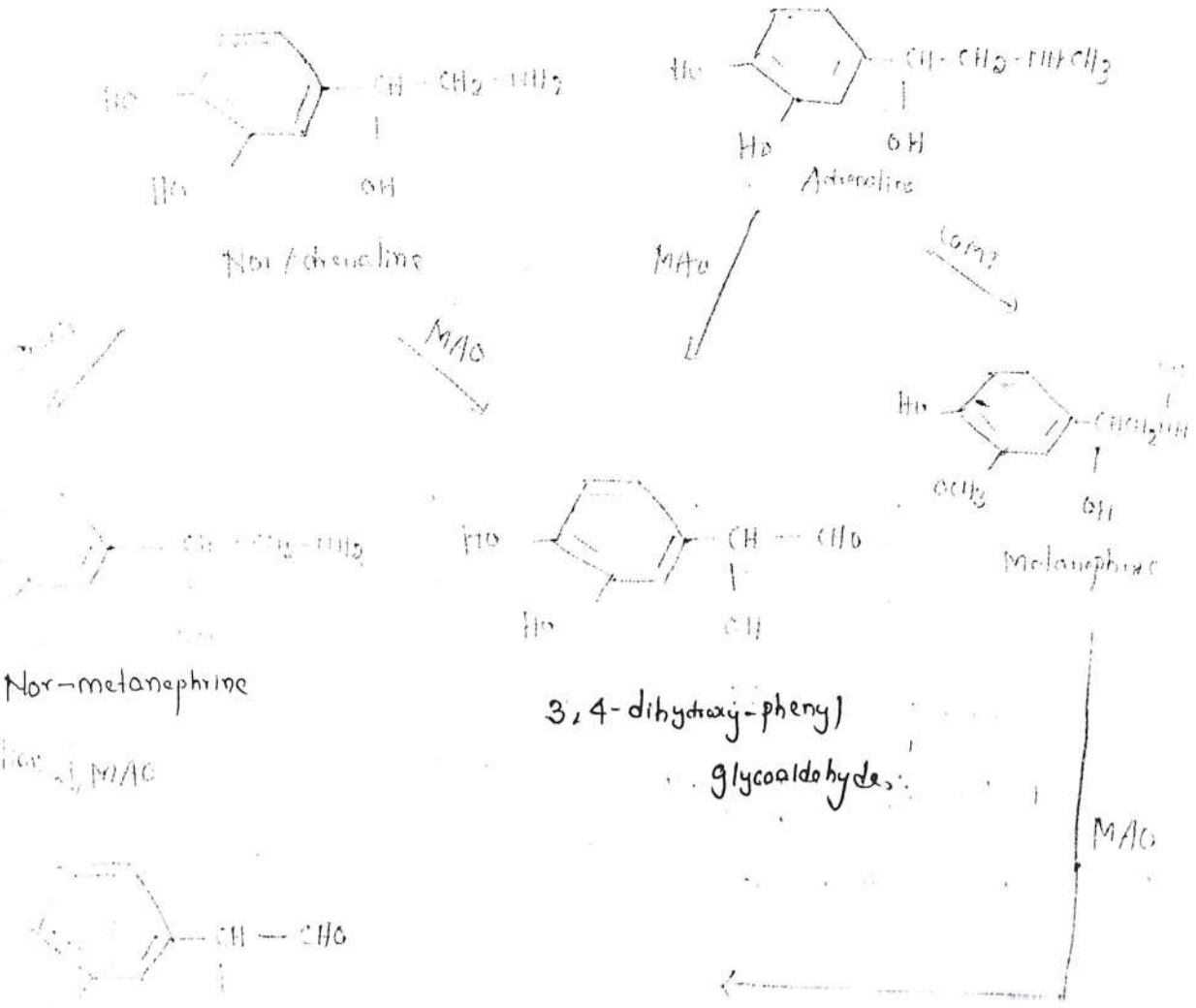


CATABOLISM OF CATECHOLAMINES

The actions of Catecholamines can be terminated through Catabolism or metabolic transformation. During this process, particular enzyme changes the structure of the Catecholamines so that they do not interact with the Receptors to produce therapeutic effects

* Two major enzymes involved in the Catabolism are

1. Mono amino oxidase (MAO)
2. Catechol O- Methyl transferase (COMT)



Adrenergic Receptors

Adrenergic Receptors are classified into two types i.e α and β receptors.

* α - Receptors are excitatory and β - Receptors are Inhibitory.

α - Receptors are categorised into α_1 and α_2 Receptors.

α_1 — Receptors are present on post synaptic Receptor sites of smooth muscles of Blood vessels and gland cells.

α_2 - Receptors are present on pre and post synaptic sites on the Nerve terminal CNS, and pancreas.

— β - Receptors are further subdivided into β_1, β_2 and β_3 Receptor.

β_1 — receptors are present in cardiac tissues ie Heart and Juxtra glomerular

- β_2- Receptors are present in Smooth muscle and gland cells ie Bronchi, Blood vessels, uterus, liver, G.I.T, eyes.
- β_3- present in Adipose tissue and urinary Bladder.

Sympathomimetic Agents

- These are chemical agents / drugs which mimics the actions of sympathetic nervous system by reacting with Adrenergic Receptors.

Classification

I. Selective α- Adrenergic agonists

a) α_1 – Agonist phenylethanolamines : Metaraminol, Methoxamine, Phenylephrine.

b) 2- Aryl imidazoline α_1-agonist :- Xylometazoline, oxymetazoline Tetrohydrozoline, Naphazoline.

c) α_2 – Adrenergic agonists

i) 2- Amino imidazolines — Clonidine, Tizanidine, Apraclonidine, Brimonidine

ii) Miscellaneous drug. — Methyldopa (α_2- Adrenergic agonist).

II. β- Adrenergic agonists.

a) Short acting β_2- Adrenergic agonists — Albuterol, Bitolterol, Cotterol.

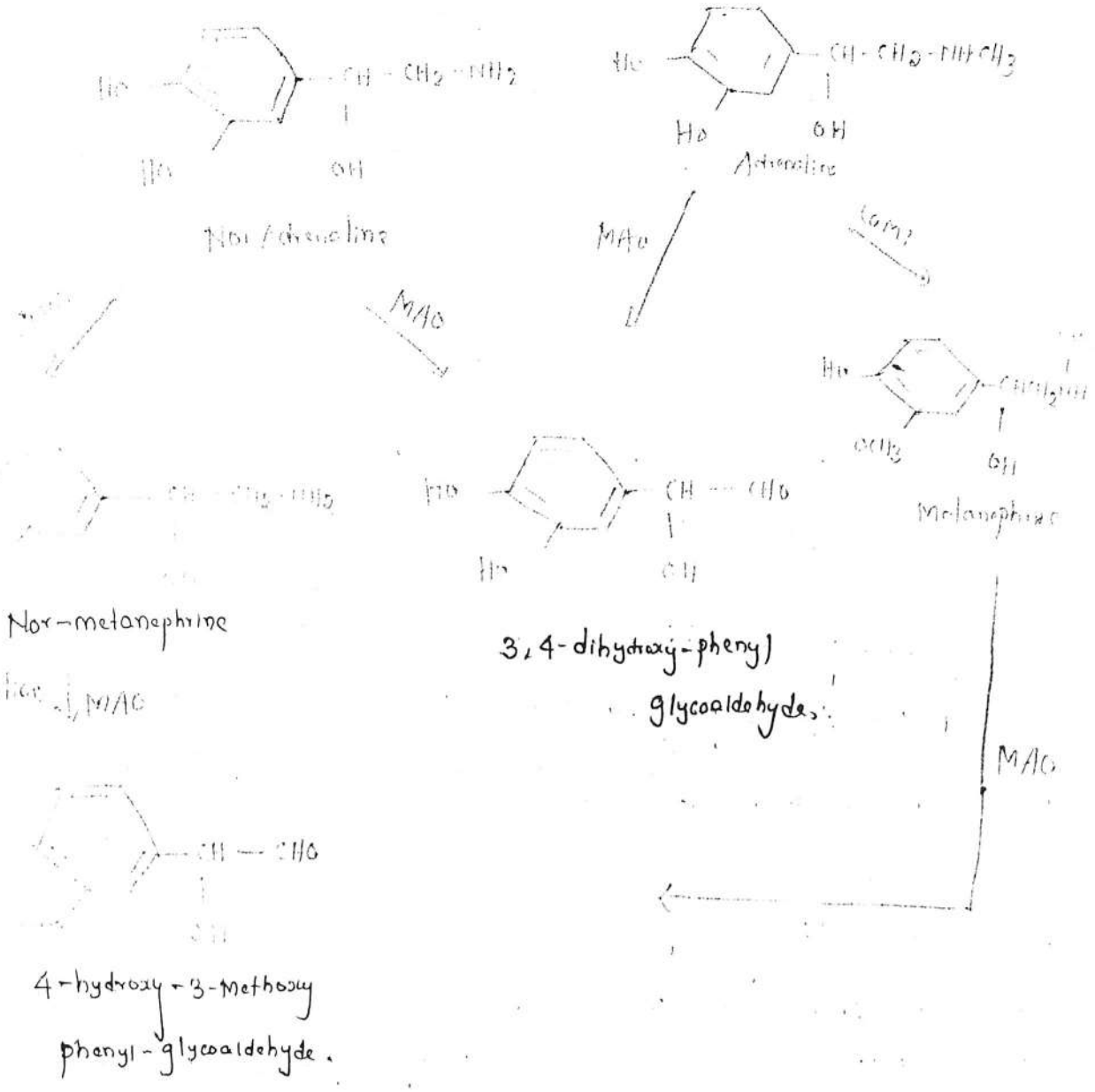
b) Long acting β_2- Adrenergic agonists — Salmeterol, Formoterol

c) β_1- Adrenergic agonists — Dopamine, Dobutamine.

III Mixed-acting sympathomimetics

a) Phenyl propanolamines — Ephedrine, Pseudoephedrine

b) Phenyl isopropyl amines — Amphetamines, Methamphetamine



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— β - Receptors are further subdivided into β_1, β_2 and β_3 Receptor.

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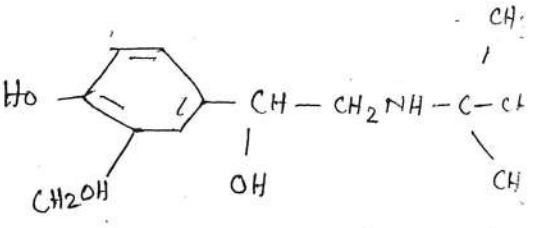
Adrenergic receptors.

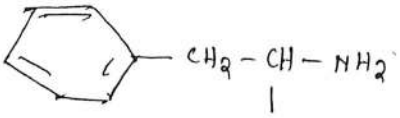
Ex;- Salbutamol is β_2-selective.



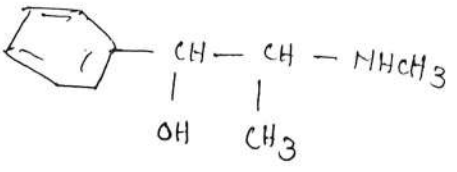
Salbutamol (β_2-selective)

4. The unsubstituted or alkyl substituted Adrenergic amines easily crosses the Blood brain barrier and have more CNS related activities.

Ex;- Amphetamine and ephedrine.



Amphetamine



Ephedrine.

B. SUBSTITUTION ON THE β-carbon

— A —OH group on the β-carbon decreases the central stimulant action due to lower lipid solubility since OH group gives polar effect / hydrophilicity. This loses agonist activity of the drug at α, β receptor.

Ex;- ephedrine has less stimulant action / effect than amphetamine but more bronchial dilation.

C. Substitution on α-carbon. — Drugs having substituent, on the α-carbon blocks the metabolism (deamination) caused by MAO and hence these have longer duration of action. Ex;- Amphetamine is resistant towards degradation by MAO.

D. Substitution on the amino group :-

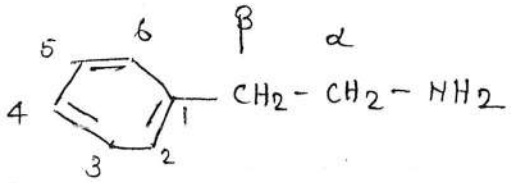
1 Lesser the substitution on the amino group, higher will be the selectivity for α-Receptors. Ex;- Adrenaline is highly α-selective than Noradrenaline.

2 More the size of alkyl substituent higher will be β-selective action. Ex- Terbutaline, Isoprenaline, salbutamol have selective β_2 activity

3 The phenyl ring must be separated from side chain amino group by 2 carbon atoms

SAR OF SYMPATHOMIMETIC DRUGS

Sympathomimetic drugs are considered as derivatives of β-phenylethylamine



β-phenyl ethyl amine (parent compound).

Structurally, substitution is possible on

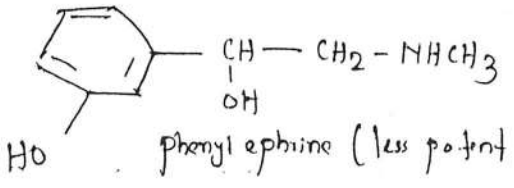
1. The Aromatic Ring
2. Substitution on β-carbon & α-carbon
3. Substitution on the Amino group.

A Substitution on the Aromatic ring of β-phenylethyl amine.

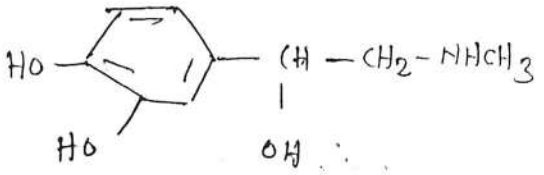
a) Effect of hydroxyl (-OH) groups:-

1. The presence of -OH group in the benzene ring at 3 and 4 positions gives maximum therapeutic (α, β) activity. If any of these -OH group is absent, the overall potency of the drug is decreased.

Ex:- phenyl ephrine is less potent than Adrenaline.



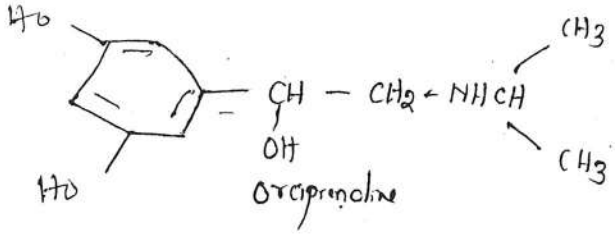
phenyl ephrine (less potent)



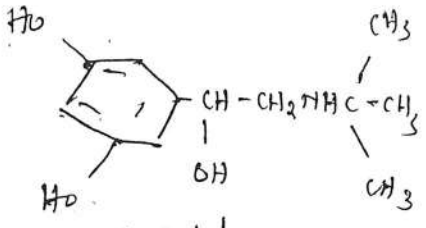
Adrenaline (more potent)

2. The presence of -OH groups at 3 and 5 position with bulky substituents on the amino Nitrogen gives β_2- Selective drug.

Ex:- Orciprenaline and Terbutaline Relaxes Bronchial muscles without effecting Cardiac muscles.

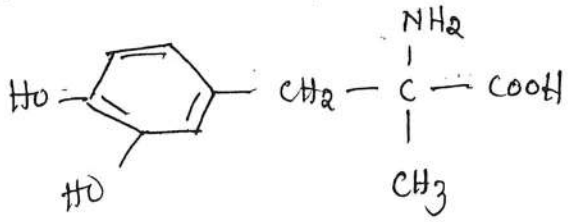


Orciprenaline



Terbutaline.

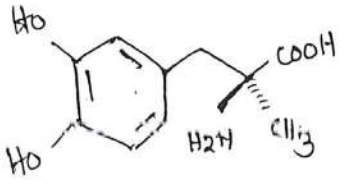
Chemical Structure :-



IUPAC Name :- 3-(3,4-dihydroxy phenyl)-2-methyl-L-alanine

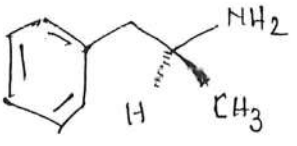
Mechanism of action :-

Methyl dopa is a prodrug which is an α_2- Agonist acting in the CNS via its active metabolite α-methyl norepinephrine.



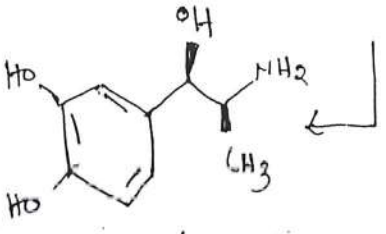
Methyl dopa

Aromatic-L-amino acid decarboxylase or Dopa decarboxylase



α-Methyl dopamine

Dopamine β-hydroxylase



α-Methyl norepinephrine.

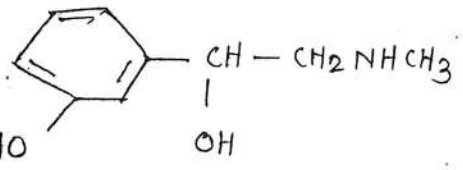
Methyldopa is transported across the Blood brain Barrier, where it is decarboxylated in the brain to α-Methyl dopamine, which is then stereospecifically hydroxylated to α-Methyl norepinephrine. It is an agonist of presynaptic CNS α_2 Adrenergic receptors. Activation of these receptors in the brain stem inhibits the output of sympathetic nervous system and lowers the blood pressure.

Uses :- (1) High Blood pressure / Hypertension

(2) Gestational hypertension / pregnancy induced hypertension

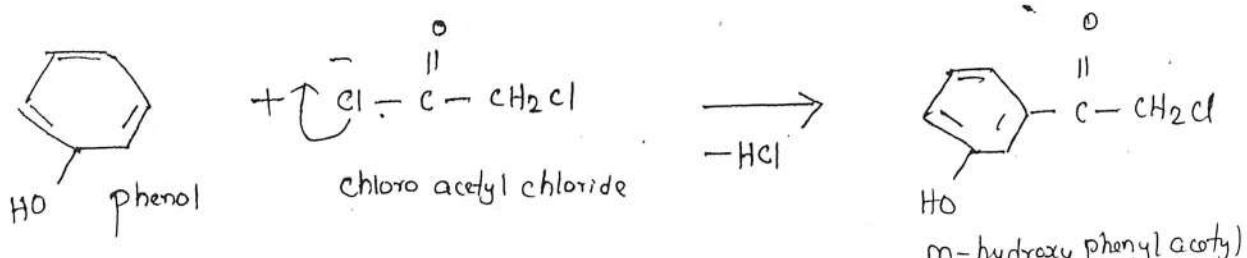
PHENYL EPHRINE

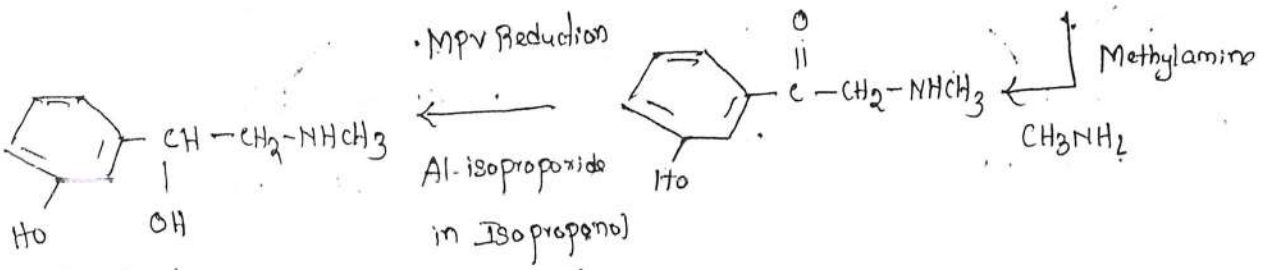
Chemical Structure



IUPAC NAME :- 2- Methylamino-1-(3-hydroxy phenyl)ethanol.

SYNTHESIS :-





phenyl ephrine.

Mechanism of action

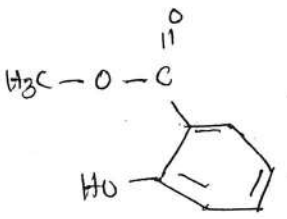
The drug shows its therapeutic action by acting as a selective α_1 Adrenergic agonist It causes vasoconstriction and increases total peripheral resistance and raises blood pressure. It also reduces intraocular tension by constricting ciliary body blood vessels and produce mydriasis.

It exerts Nasal decongestant action by vasoconstrictory action on arteries of nasal mucosa It prolongs and localises the action of anesthetic due to its vasoconstrictory action

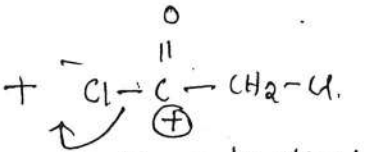
Adverse effect — primary side effect of phenyl ephrine is high blood pressure.
- Prostatic hyperplasia (↑se in size of prostate gland)

uses :- (1) Decongestant — oral medicines / nasal spray
2. Treatment of hemorrhoids / piles
3 used as an eyedrop to dilate the pupil to improve the

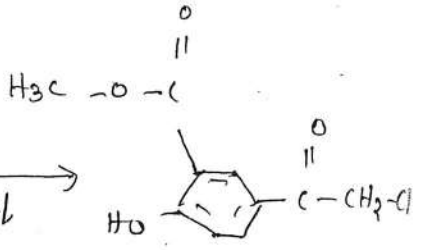
Synthesis :-



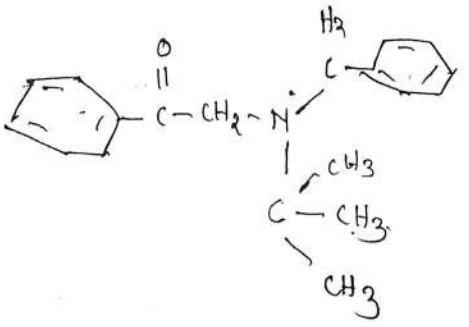
2-hydroxy-Benzoic methyl ester

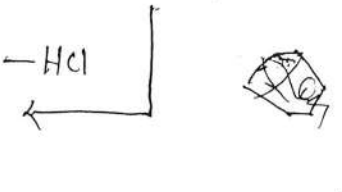


chloro acetyl chloride

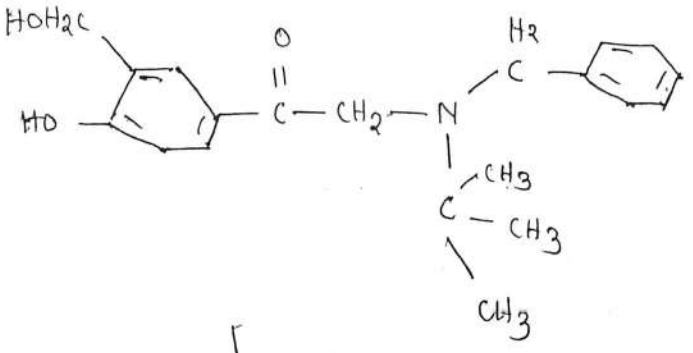


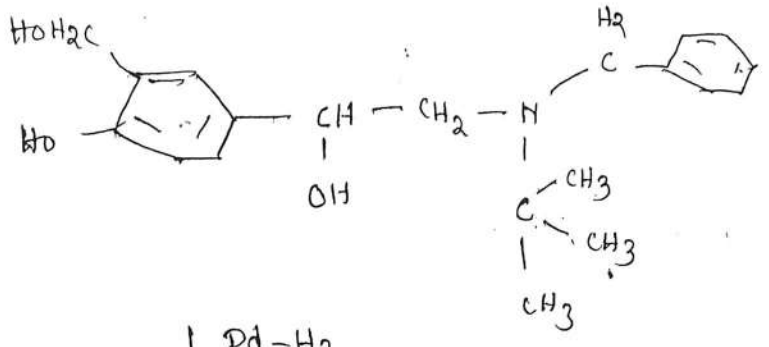
5-(2-chloro acetyl)-2 hydroxy-Benzoic acid methyl ester.

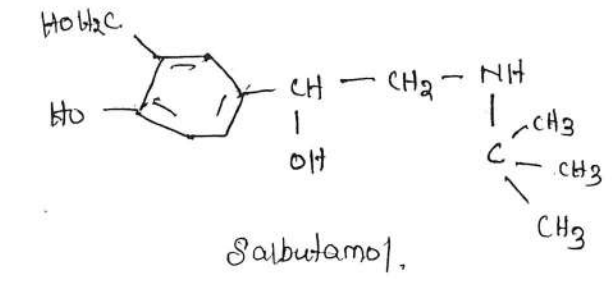




Benzyl tert-butyl amine.



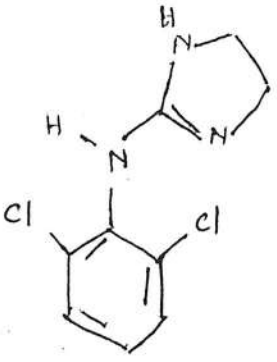




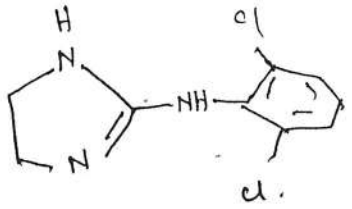
Salbutamol.

Clonidine

Chemical structure



or



Belongs to imidazoline class of Sympatholytic agent. It is a central α-2 Adrenergic agonist

Mechanism of action

Clonidine is an imidazoline derivative and centrally acting α-adrenergic agonist, with anti hypertensive activity.

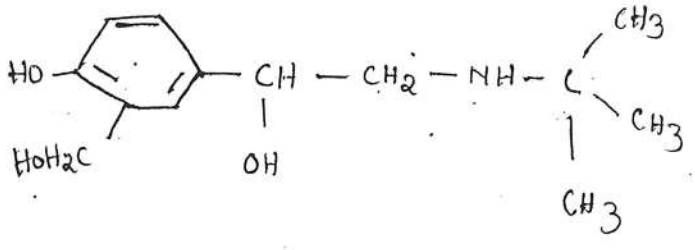
Clonidine binds to and stimulates central alpha-2-adrenergic receptors, thereby reducing the amount of norepinephrine (NE) release and thus decreasing sympathetic outflow to the heart, kidneys and peripheral vasculature. The reduction in sympathetic outflow leads to decreased peripheral vascular resistance, decreased blood pressure and slowed heart rate.

Uses:
1. It is used to treat Hypertension.
2. Attention deficit Hyperactivity disorder (ADHD)
3. Diarrhoea and certain pain conditions
4. Menopausal flushing / Menopause.

ADR – Sedation, Drymouth, low B.P, orthostatic hypotension / postural hypotension (B.P falls down suddenly standing up from lying / sitting position).

Salbutamol / Albuterol

Chemical structure :-

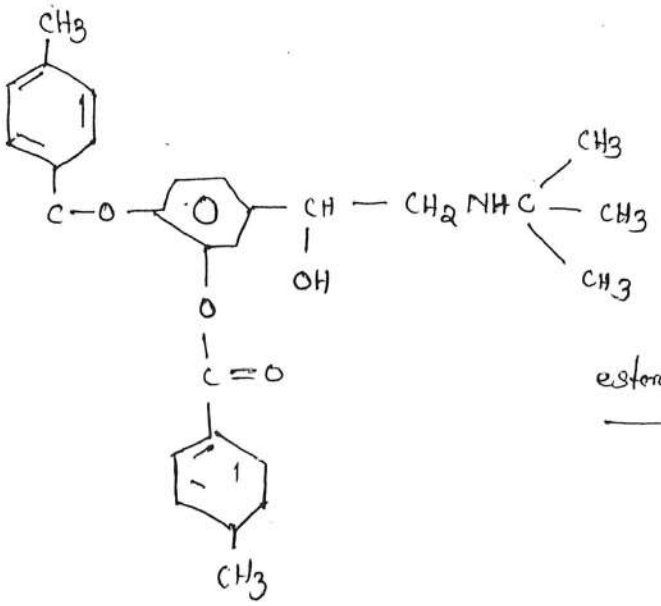


Bitolterol

— Bitolterol is a prodrug form of Colterol in which hydroxyl groups have been converted to 4-methyl benzoic acid esters, providing ↑ed lipid solubility and prolonged duration of action.

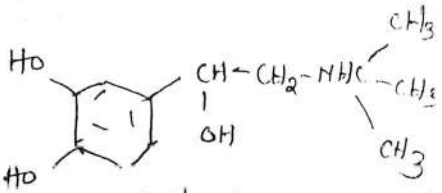
— Ester groups are hydrolysed in the presence of esterases to liberate the active drug Colterol

Onset of action - 2-5 min
Duration of action - 6-8 hr



Bitolterol

esterases →



Colterol

MOA — Similar to Salbutamol — Bitolterol is a diester sympathomimetic amine with Bronchodilator activity. As an ester prodrug, bitolterol is hydrolysed by esterases to its active metabolite Colterol. Colterol selectively binds and activates β_2-Adrenergic Receptors in Bronchial smooth muscle thereby, causing stimulation of Adenyl cyclase, the enzyme that catalyses the conversion of ATP to Cyclic AMP. ↑ed intracellular cyclic AMP causes relaxation of Bronchial smooth muscle. This increase air flow and prevents bronchospasm and may eventually leads to an improvement of airway function.

Uses: ① Asthma
② COPD.

Chemistry — Salbutamol is sold as Racemic mixture. The (R) enantiomer is responsible for the pharmacological activity whereas (S) enantiomer blocks metabolic pathways associated with elimination.

— Tertiary butyl group in albuterol / salbutamol makes it more selective for β_2 - Receptor.

Mechanism of action

Salbutamol stimulates β_2 - Adrenergic receptors which are predominant receptors in Bronchial smooth muscles.

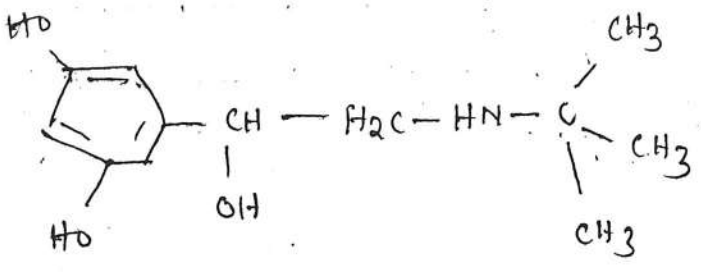
* Stimulation of β_2 - Receptors leads to the activation of enzyme Adenyl Cyclase (catalyses the conversion of ATP to) that forms cyclic AMP (Adenosine - Mono phosphate). This increase in cyclic AMP Relaxes Bronchial smooth muscle and decreases airway resistance by lowering intracellular ionic Calcium Concentrations.

— Used cyclic AMP contractions are also inhibit the Broncho constrictor mediators like histamine, leukotriene from the mast cells in the airway.

USES — It is used in the treatment of Asthma
— Chronic obstructive pulmonary disease (COPD)
— treatment of acute hyperkalemia as it stimulates potassium flow into the cells thus lowering the conc. in the blood.

— Route of Administration — Inhaler / Nebuliser (drug delivery device)

TERBUTALINE — MOA similar to salbutamol



— Tertiary butyl groups makes it more selective for β_2 - Receptors

Uses:- 1. Fast-acting Bronchodilator often used in the treatment of Asthma

that occurs during anaphylaxis which can cause the loss of intravascular fluid volume.

* This drug also produces an increase in blood sugar and increases glycogenolysis in liver. Through its action on β-Adrenergic Receptors, it leads to Bronchial smooth muscle Relaxation that helps to Relieve bronchospasm, dyspnea that may occur during anaphylaxis.

* Adrenaline acts by binding to a variety of Adrenergic Receptors. Adrenaline is a non selective agonist of all Adrenergic Receptors, including the $\alpha_1, \alpha_2, \beta_1, \beta_2, \beta_3$. Adrenaline binding to these receptors triggers a number of metabolic changes.

(1) Binding to α-Adrenergic Receptors inhibits insulin secretion by the pancreas
(2) Stimulates glycogenolysis in liver and muscle
(3) Stimulates glycolysis and inhibits insulin-mediated glycogenesis in muscle

β-Adrenergic binding (Receptor) triggers

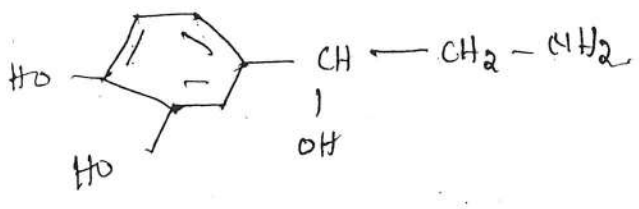
(1) glucagon secretion in pancreas
(2) ↑ed Adrenocorticotropic hormone (ACH) by pituitary gland
(3) ↑ed lipolysis by Adipose tissue.

Together all these effects leads to ↑ed Blood glucose and fatty acids providing substrates for energy production within cells throughout the body

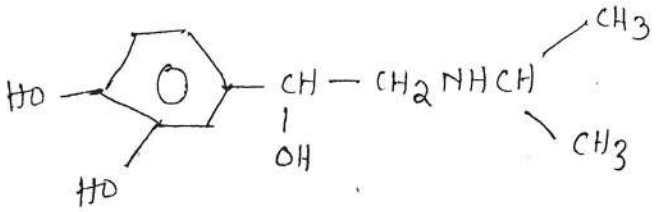
— It also ↑ses peripheral resistance, causes Vasoconstriction, ↑s Cardiac output by binding with β-receptor.

— Uses — used in emergencies to treat life threatening Serious Allergic reactions to insect stings / bites, foods, drugs or other substances
— Relaxes bronchial smooth muscles in the treatment of Asthma
— management of glaucoma as it lowers intraocular pressure

Norepinephrine



Isoprenaline / Isoproterrenol.



Isopropylamine group in isoprenaline makes it more ~~susceptible~~ selective for β-Receptors. The free catechol hydroxyl groups keeps it susceptible for enzymatic metabolism.

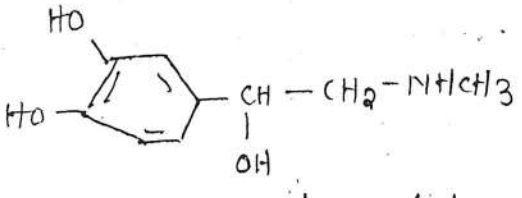
It is a nonselective β-Adrenergic Receptor agonist therefore it can bind with both β_1-Receptors (heart) and β_2-Receptors (Bronchial smooth muscles)

uses
1. It is used to treat heartblock and episodes of Adams Stokes Syndrome, Bradycardia (slow heart rate)
2. Sympatomatic Relief for Asthma.
3. Cardiac stimulant.

MOA:- Isoprenaline exerts its pharmacological action by acting as nonselective β-adrenergic agonist. It causes Bronchodilation, Cardiac stimulation and peripheral vasodilation. By its direct action on β_2-Adrenergic Receptors it relaxes bronchial smooth muscles, relieving Bronchospasm, ↑ing vital capacity, ↓ing Residual volume in lungs and facilitating passage of pulmonary secretions. It exerts cardiac stimulant action by action on β_1-adrenergic receptors and produces +ve chronotropic and inotropic effects

(↑ in the heart rate) ↓ (↑ in cardiac contractions)

Epinephrine

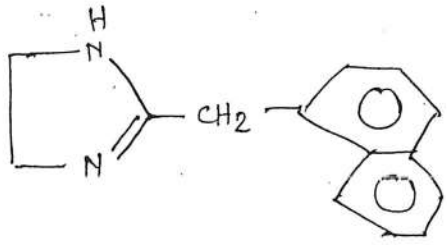


MOA → Epinephrine acts on Alpha and Beta Receptors and is the strongest Alpha Receptor activator. when it binds with α-Receptors it minimises the Vasodilation and ↑ed vascular permeability

inadequate blood flow due to the dysfunction of the ventricles of the heart.

2. Severe Heart failure.

Naphazoline

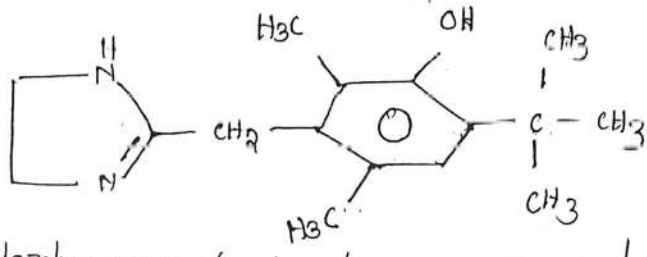


Mechanism of action

Upon ocular administration, Naphazoline exerts its action/effect by acting on α-adrenergic receptors in the arterioles of conjunctiva to produce vasoconstriction, resulting in decreased conjunctival congestion and diminished itching, irritation and Redness.

Uses — Solution of Naphazoline is used in the eyes as conjunctival decongestant

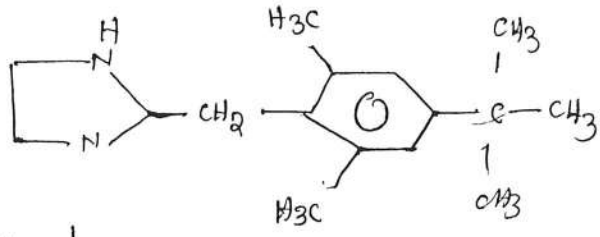
Oxymetazoline



Mechanism Oxymetazoline is a direct acting sympathomimetic amine which acts on α-adrenergic receptors in the arterioles of the conjunctiva and nasal mucosa. It produces vasoconstriction, resulting in decreased conjunctival congestion in eye. In nasal, it produces constriction, resulting in decreased blood flow and decreased nasal congestion

Uses — used as a topical decongestant in the form of nasal spray (otrivin)
— Treatment of persistant facial erythema (redness)
— Treatment of Nose bleeds and eye redness due to minor irritation.

Xylometazoline



Mechanism — Similar to oxymetazoline

Uses — 1. Nasal Decongestant 2. Allergic Rhinitis 3. Sinusitis

Caution — Contraindicated in high Blood pressure patients and Cardiac problems

Mechanism of action

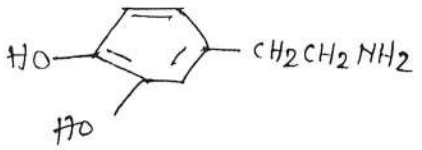
It stimulates α_1, and α_2 Adrenergic receptors to cause blood vessel contraction, thus ↑es peripheral vascular resistance and resulted in ↑ed Blood pressure.

It also acts on β_1 – adrenergic Receptors, causing increase in heartrate and cardiac output.

uses:- Treatment of hypotension.

decreases the chances of haemorrhage during an operation

Dopamine :-



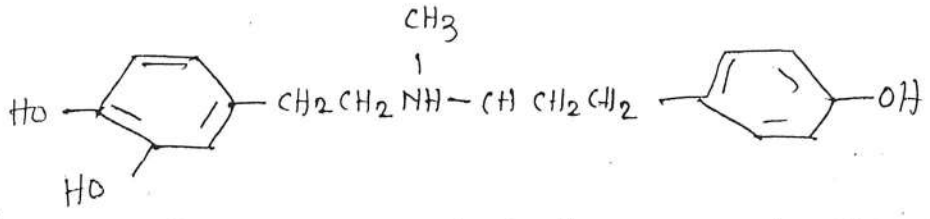
Mechanism of action — Dopamine is a precursor to Norepinephrine in noradrenergic nerves and is also a neurotransmitter in certain areas of the CNS.

Dopamine produces +ve chronotropic and ionotropic effects on the myocardium, resulting in increased heart rate and cardiac contractility. This is accomplished directly by exerting an agonist action on Beta-receptors and indirectly by causing release of norepinephrine, from storage sites in sympathetic nerve endings by binding indirectly with α- Adrenergic Receptors

uses:- used in severe congestive Heart failure where it increases BP and urine outflow

- used intravenously in myocardial infarction, trauma, cardiac surgery.

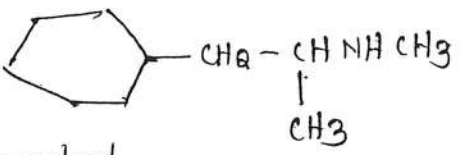
Dobutamine



Mechanism of action — Dobutamine is a direct acting agent whose primary activity results from stimulation of the β_1- Adreno receptors of the heart, increasing contractility and cardiac output. Unlike Dopamine, it will not release norepinephrine & so the blood pressure is not elevated.

* Dobutamine is administered as Racemic mixture consisting of (+) and (-) isomers.

(+) isomer – potent β_1- agonist and α_1- antagonist



Uses :- 1. Nasal Decongestant — Colds, Allergies and Allergic Rhinitis
2. Appetite suppressant
3. psychostimulant.

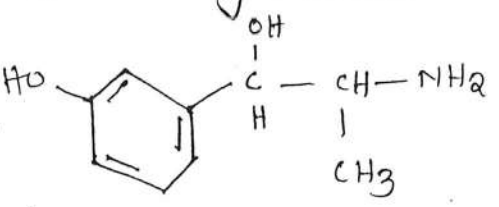
— propyl hexedrine is a chiral compound and sold as Racemic (RS) - Propylhexidrine

— levo propyl hexedrine is biologically active than dextro
more

Mechanism of action — propylhexidrine causes the NorepiNephrine, dopamine and Serotonin transporters to reverse their direction of flow. This inversion leads to a release of these transmitters from the vesicles to the cytoplasm and from cytoplasm to the synapse. Additionally, propyl hexedrine appears to antagonize the Vesicular Monoamine transporter 2 (VMAT-2), leading to further increase in monoamines.

~~Mixed acting sympathomimetic drugs~~

Metaraminol



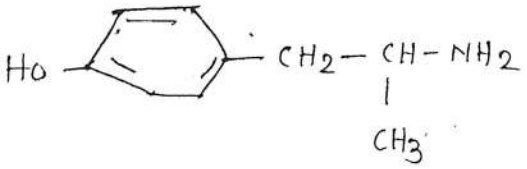
2-amino-1-(3-hydroxy phenyl)-propan-1-ol.

Mechanism of action — Metaraminol acts through peripheral Vasoconstriction by acting as pure α_1- adrenergic Receptor agonist, consequently increasing systemic blood pressure (both systolic and diastolic). Its effect is associated with the inhibition of adenyl cyclase which leads to inhibition of the production of CAMP. Another effect of metaraminol is that it releases ~~ep~~ noreprinephrine from its storage site indirectly.

uses — · Prevention and treatment of hypotension.

Indirectly acting sympathomimetic drugs

1. HYDROXY AMPHETAMINE



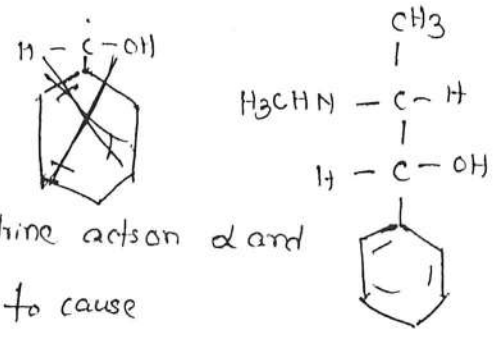
Mechanism of action

It is an indirect acting sympathomimetic agent which cause the release of Norepinephrine from adrenergic nerve terminals, resulting in ~~mydriasis (dilation of pupil size)~~. stimulation of α & β - adrenergic Receptors. Local α-stimulatory effects include dilation of pupil, increased flow of aqueous humor, and vasoconstriction.

uses — 1. used in eyedrops to dilate the pupil (Mydriatic)

2. used as diagnostic agent for testing Horners syndrome (damage of nerves of eyes).

2. Pseudoephedrine



Mechanism

Pseudoephedrine acts on α and β_2 Adrenergic Receptors to cause vasoconstriction and Relaxation of smooth muscles. α- Adrenergic Receptors are located on the muscles lining the walls of blood vessels. When these receptors are activated, muscles contract, causing the blood vessels to constrict (vasoconstriction). The constricted blood vessels now allow less fluid to leave the blood vessels and enter the Nose, throat and sinus linings, which results in decreased inflammation of nasal membranes as well as decreased mucus production. Hence it acts as Nasal decongestant.

- Activation of β_2- adrenergic receptors produces relaxation of smooth muscle of the bronchi causing bronchial dilation and in turn decreasing congestion and difficulty in breathing.

Uses

(1) Nasal / sinus decongestant

(2) Stimulant / wakefulness promoting agent in higher dose.

a) Non Selective α-Adrenergic antagonist

i) Haloalkylamines — phenoxybenzamine

ii) Imidazolines — Tolazoline, phentolamine

b) α_1-selective antagonist — prazocin

c) α_2-selective antagonist — Yohimbine

d) Ergot alkaloids — Dihydroergotamine, Methyl sergide

— α_1-Receptors mediates the actions of catecholamines and causes contraction of arterial and venous smooth muscles. α_2-Receptors regulate the activity of sympathetic nervous system. So α_1 Blockers inhibit vasoconstriction and causes fall in Blood pressure

Effects of α_1-blocking agent

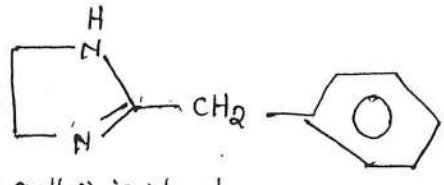
1. Reduced Blood pressure, causes nasal congestion
2. enhances Venous capacitance
3. Produces miosis and interference with ejaculation
4. Increased secretion of renin, tachycardia and palpitations.

Imidazolines — The imidazoliner α-antagonists are reversible ie competitive blockers. Their structures are similar to that of imidazoline α-agonist drug

ex:- Naphazoline / xylometazoline / oxymetazoline.

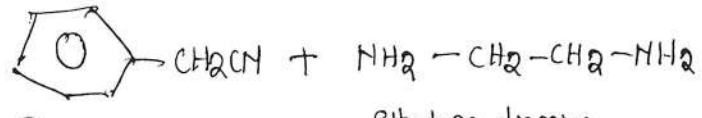
— Two drugs of the imidazoline α-Blockers are Tolazoline & phentolamine

Tolazoline



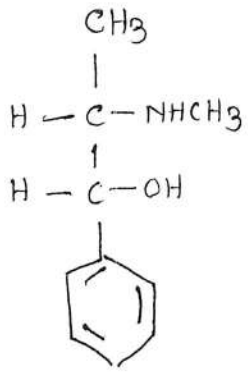
IUPAC Name: 4,5-dihydro-2(phenyl methyl) imidazole

Synthesis - It is the prepared by the reaction of 1mole of benzyl cyanide and 1mole of ethylene diamine in the presence of carbon disulphide

a) 

Benzyl Cyanide — Ethylene diamine — Tolazoline

Ephedrine



(−) Ephedrine

Mechanism of action — Ephedrine is a mixed adrenergic agonist that directly binds and activates α and β-adrenergic receptors as well as causing release of endogenously stored nor-epinephrine from presynaptic terminals

Direct Adrenergic activation — ephedrine binds with α & β-adrenergic Receptors including α_1, β_1, β_2 Receptors. As a result, administration of the drug stimulates sympathetic nervous system. Also causes systemic vasoconstriction, combined with enhancement of cardiac contractility and heart rate via β_1-Receptors. As a result it causes tachycardia & hypertension

Indirect Adrenergic Activation — ephedrine also results in release of stored norepinephrine from adrenergic neuron nerve terminals into the synaptic cleft, contributing to non specific activation of sympathetic nervous system

Uses: (1) prevent low Blood pressure during spinal anesthesia

(2) Asthma

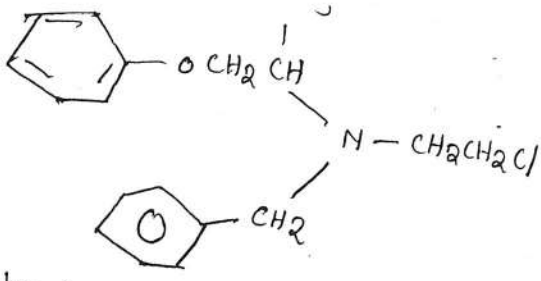
(3) Nasal decongestant (4) Mydriatic

α- Adrenergic Blockers

~~Phentolamine~~ These drugs are competitive inhibitors of the effects of Catecholamines at α- Adrenergic Receptors.

Classification of α- Adrenergic Blockers

— Non-Selective irreversible α-Blocker.



— Mechanism of action

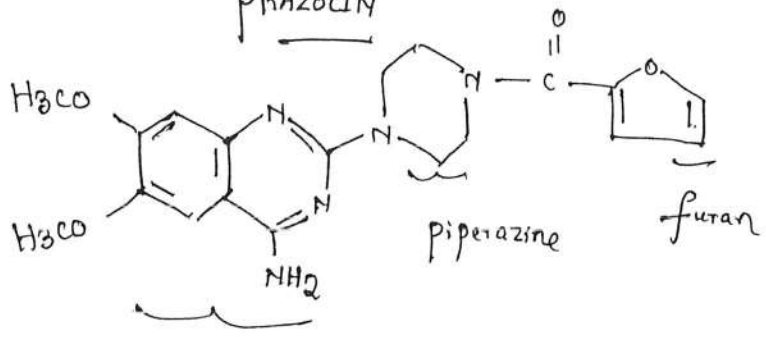
Phenoxybenzamine forms a permanent covalent bond with Adrenergic receptors. Then it remains permanently bound to the receptor, preventing Adrenaline and noradrenaline from binding. This causes Vasodilation in Blood vessels and as a Result lysed B.p

— As a Non Selective α-Receptor antagonist, it will affect both the post synaptic α_1 and presynaptic α_2 receptors in the nervous sysbro, and reduces Sympathetic activity This result in further Vasodilation, pupil constriction, lose in GI tract motility and secretions.

Uses — It is used in the treatment of hypertension caused by Pheochromacytoma

— Treatment of benign prostatic hyperplasia

PRAZOCIN



use — treatment of high B.p
- Heart failure and Raynaud's Syndrome.
- Symptomatic treatment of urinary obstruction by prostatic hypertrophy

Mechanism of action — Prazocin is a α_1-Blocker that acts as an inverse agonist at α_1-Adrenergic Receptors. These Receptors are found on ~~adrenergic~~ Vascular smooth muscle, where they are responsible for vasoconstrictive action of norepinephrine. They are also found throughout CNS.

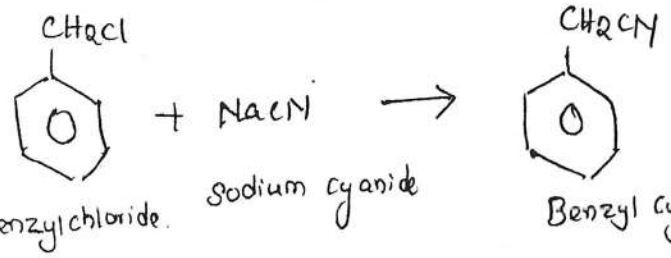
(or)

Prazocin acts by inhibiting post synaptic α_1-Adrenoreceptors on Vascular smooth muscle. This inhibit the vasoconstrictor effect of circulating and locally released Catecholamines (epinephrine and norepinephrine) and causes peripheral vasodilation and drop in Blood pressure.

* INVERSE AGONIST — A drug that binds to some Receptor as an agonist but induces pharmacological response opposite to that agonist

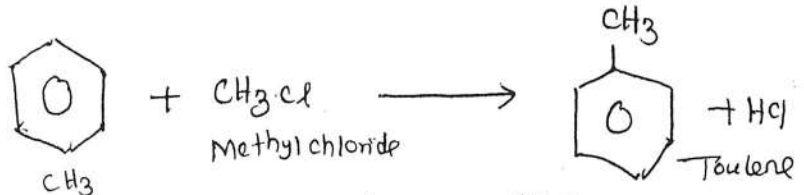
— Benzyl cyanide can be produced via Kolbe-nitrile Synthesis between benzyl chloride and sodium cyanide

(3)

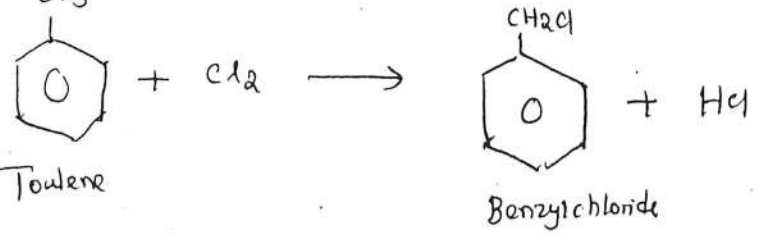


Benzene

(1)



(2)



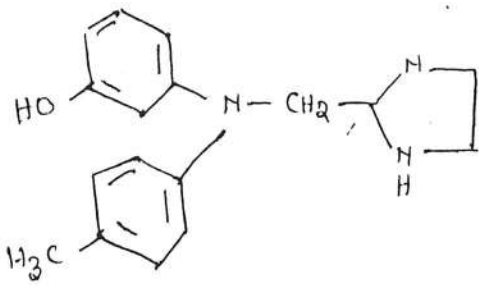
Mechanism of action — It is a Competitive Inhibitor of α-Receptor. Its structure is similar to that of α-agonist so, it can bind reversibly with α-Receptor (in place of α-agonist) and blocks the effects of α-receptors. It causes Vasodilation of the Blood Vessels and decreases the Blood pressure, Also total peripheral resistance.

Uses: Treatment of pulmonary hypertension of the newborn.

— improves pulmonary circulation in ventilated babies.

2. Phentolamine

— Reversible Nonselective Adrenergic antagonist.



Uses:- It is used to control hypertension associated with pheochromacytoma

Mechanism of action

Phentolamine produces its therapeutic actions by Competitively blocking α-adrenergic Receptors, leading to muscle relaxation and widening of blood vessels. This widening of blood vessels result in lowering of blood pressure. The action of phentolamine on α adrenergic Receptor is transcient and the blocking effect is incomplete. The drug is more effective in antagonising responses to Circulating epinephrine (not Epinephrine) It also Stimulate β-adrenergic receptor +ve ionotropic and chronotropic effect on the

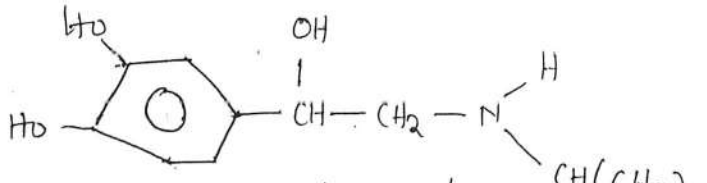
β-Blockers are competitive inhibitors of the effects produced by catecholamines at β-receptor site.

Classification of β-Blockers

1. β_1 – selective blocker — Atenolol, Betaxalol, Bisoprolol, Esmolol, Metoprolol

SAR of β-Blockers

SAR of Arylethanolamines



Isoproterenol / Isoprenaline.

Various modifications have been made to the structure of isoproterenol.

1. Phenolic / catechol OH groups are important for agonist activity. Replacement of 4-OH group by other groups leads to abolishing of agonist activity and makes the compound antagonist.

   Ex: Replacement of catechol OH groups by chlorine gives dichloro isoproterenol, which is the first useful β-Blocker.

2. The two carbon side chain is required for the activity. It cannot be decreased / increased.

3. Small substituents on N produces α-activity, for β-activity larger groups must be substituted on 'N'. Various substitutions on 'N' are as follows.

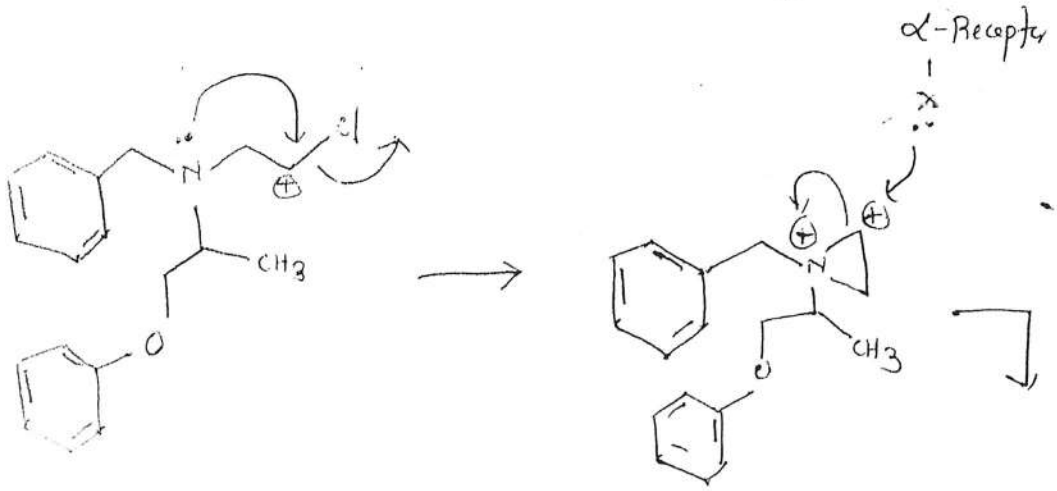
a) N, N – disubstituted compounds are inactive

b) Phenyl ethyl, hydroxy phenyl ethyl groups when added to N maintain β-Blocker activity

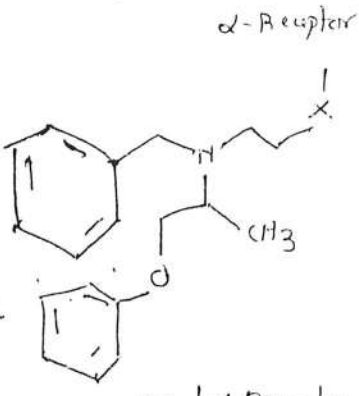
c) Cyclic alkyl substitution provides better pharmacological activity than open

~~Ergot alkaloids~~ Molecular level of Mechanism of phenoxybenzamine

Phenoxy benzamine alkylation of α-adrenoreceptor



- phenoxybenzamine is a β-haloalkylamine that alkylates α-Receptors.
- The unshared electrons of the unprotonated amino group act nucleophilic and displace the β-chlorine atom in the intramolecular reaction to form highly reactive "aziridinium ion"



Alkylated Receptor

If this occurs in the viscinity of an α-Receptor, a nucleophile group 'X' on the Receptor can open the aziridinium ion in an nucleophilic reaction to form a covalent bond between the Receptor and the drug. The substituents attached to the haloalkylamine provide selectivity for binding to α-adrenoreceptors so that nucleophile generally is part of target Receptor.

- The Nucleophile X is part of an amino acid side chain such as cysteine thiol, Serine hydroxyl, lysine amino group etc. phenoxybenzamine forms covalent bonds with the receptor is irreversible, new receptor must be synthesized before the effect can be overcome. Therefore, α-blockade is long lasting
- unfortunately, other biomolecules besides the target α-receptor also are alkylated. because of its Receptor nonselectivity and toxicity, the use of phenoxybenzamine is limited to the treatment of pheochromocytoma. This tumor of chromaffin cells of adrenal medulla produces large amounts of epinephrine and norepinephrine

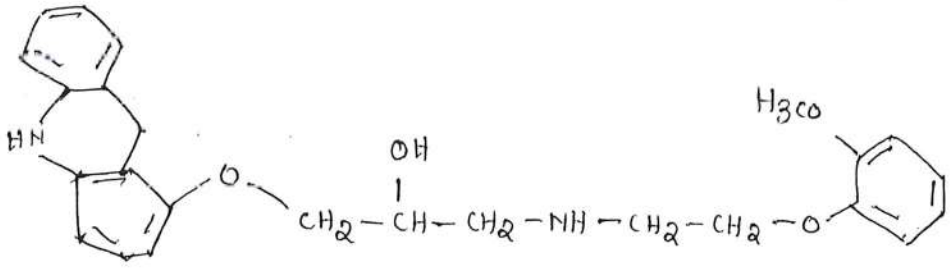
Classification of β-Blockers

Selective β_1 — Acebutolol
Atenolol
Bisoprolol
Celiprolol
Metoprolol
Nebivolol

Non selective β_1 & β_2 Blockers — Esmolol
Oxprenolol
Pindolol
Propranolol
Sotalol
Timolol

Mixed α & β-Blockers — Carvedilol
Labetolol.

CARVEDILOL



Mechanism of action — Carvedilol is both non-selective β-Adrenergic Receptor blocker (β_1, β_2) and an Alpha adrenergic receptor blocker (α_1).

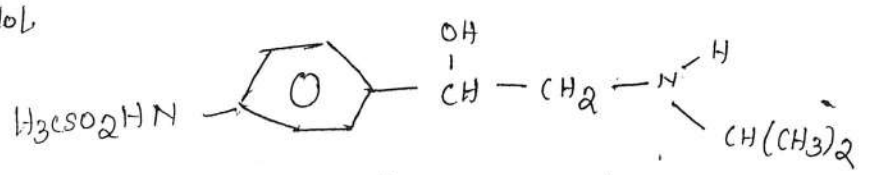
- The S(-) enantiomer accounts for the β-Blocking activity whereas S(-) and R(+) enantiomer have α-blocking activity.
- Carvedilol Reversibly binds to β-receptors on myocytes. Inhibition of these receptors prevents a response to the sympathetic nervous system, leading to decreased heart rate and contractility.
- Blockade of α_1-receptors causes Vasodilation of blood vessels. This inhibition leads to decreased peripheral vascular resistance and antihypertensive effect can be observed.

open chain substituent at 'N' atom of amine.

d) α- methyl substitution can lose the activity

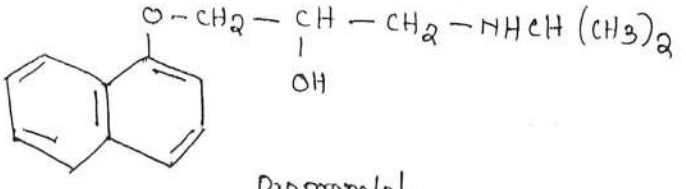
4. phenolic-OH group substitution on the phenyl ring can be replaced by methyl sulfonamide to lose the activity

Ex:- Sotalol



P-OH group on phenyl ring can also be replaced by nitro group to produce good activity,

b) SAR of Aryloxy propanolamines — more potent than aryl ethanolamines



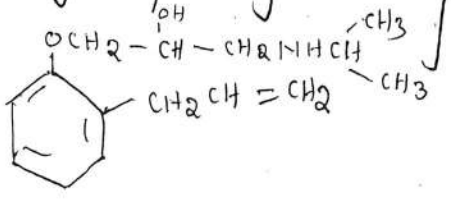
propranolol.

Various modifications have been done to alter the activity of aryloxy propanolamines.

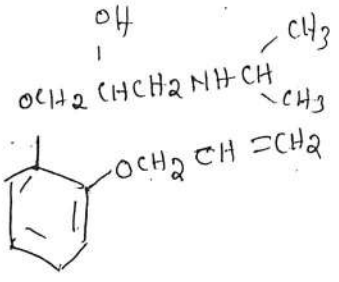
1. The O-CH2 group is placed between the aromatic ring and the ethanolamine side chain, which is essential for activity.

2. lengthening the sidechain would prevent appropriate binding of the required functional groups to the same Receptor site. So the Biological activity also decreases

3 Alkenyl and Alkenyloxy groups when present in the ortho position on the phenyl ring, given good β-antagonist activity.



Alprenolol



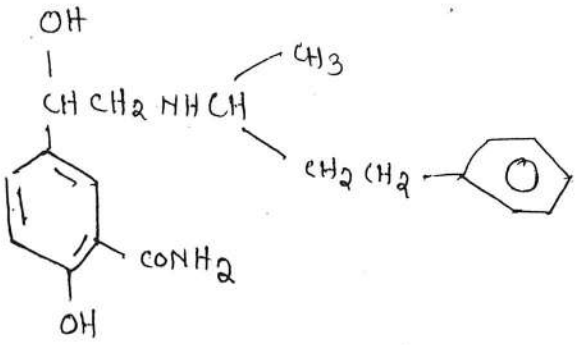
Oxprenolol

4 Isopropyl and t-butyl groups present on the amine group provides nucleophilicity to the amino amine, hence

Uses:- (1) It is used in the management of [illegible]

(2) treatment of hypertension.

Labetolol

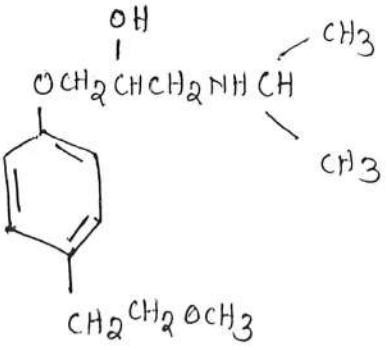


Uses:- Management of hypertensive emergencies, post operative hypertension

— Treatment of pregnancy induced hypertension.

-- No Membrane stabilising activity.

Metoprolol



Mechanism of action

Metoprolol is a beta-1 Adrenergic Receptor inhibitor specific to cardiac cells with negligible effect on β_2-Receptors. This inhibition decreases caediac output by producing negative chronotropic and ionotropic effect without presenting activity towards membrane stabilisation nor intrinsic sympathomimetic.

Uses: 1. It is Antihypertensive

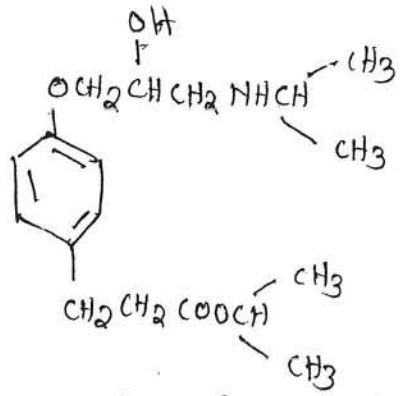
2. Management of cardiac asrythmia & angina pectoris

3 Management of acute myocardial infarction

MoA 2 Metoprolol blocks β_1 – Adrenergic Receptors in heart muscle cells, thereby lising the slope of phase 4 in the nodal action potential (reducing Na^+ influ and prolonging repolarisation of phase 3 (slowing down K^+ release).

← It also suppresses the nor-epinephrine-induced increase in the sarcoplasmic reticulum Ca^{2+} leak and the spontaneous SR Ca^{2+} release, which are the major triggers for Atrial fibrillation.

Esmolol



— lacks intrinsic Sympathomimetic and membrane stabilising activity.

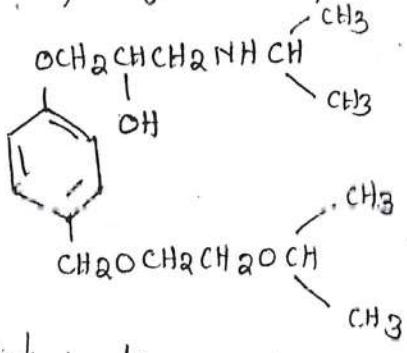
MOA — It decreases the force and rate of contractions by blocking Beta-adrenergic receptors of the sympathetic nervous system, which are found in heart and other organs of the body.

— It prevents the actions two naturally occuring substances; epinephrine and norepinephrin

Uses:-

1. Treatment of Supraventricular Tachycardic
2. Treatment of high Blood pressure during and after cardiac surgery
3. Management of Atrial fibrillation
4. Early treatment of myocardial infarction

Bisoprolol

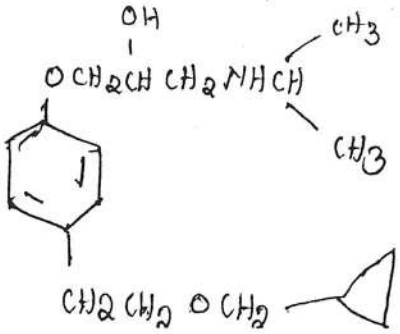


MOA — Bisoprolol selectively blocks Catecholamine stimulation of β_1-adrenergic receptors in the heart and Vascular smooth muscle. This result in reduction of heart rate, cardiac output, systolic and diastolic blood pressure and possibly reflex orthostatic hypotension.

Uses Treatment of high B.P

— Management of Cardiac ischaemia ie reduced blood flow to the heart.

Betaxalol



MOA similar to Bisoprolol,

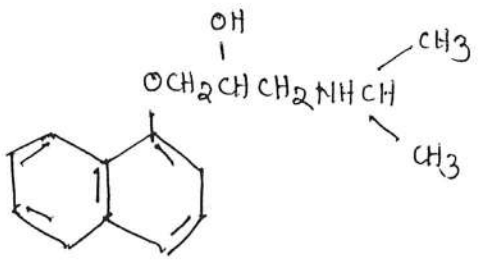
— lacks Sympathomimetic ~~or~~ but little membrane stabilising

potentially cause bronchospasm, dyspnea and respiratory failure, especially in patient with asthma or COPD.

— Metipranolol also reduces intraocular pressure primarily by blockade of β-receptors in the ciliary epithelium of the eye, which lowers aqueous humor production.

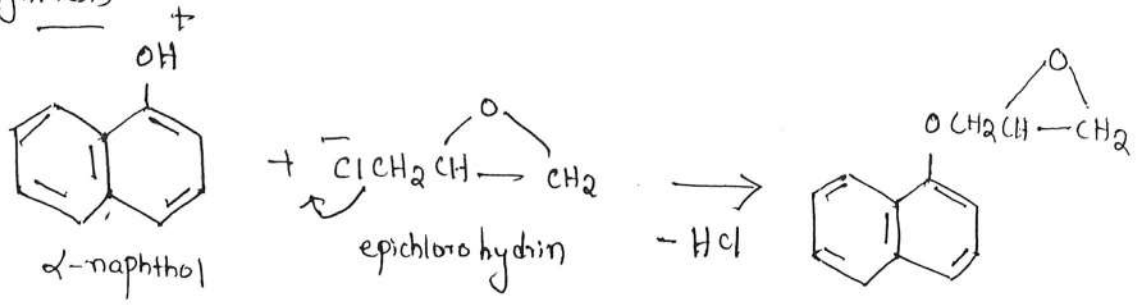
uses:- used in eyedrops in the treatment of glaucoma

PROPRANOLOL

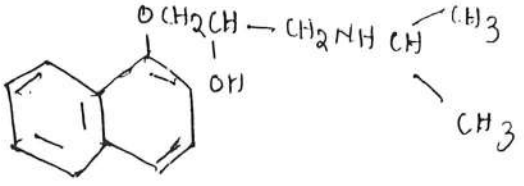


IUPAC Name (RS)-1-Isopropylamino-3-(1-naphthyloxy) propan-2-ol.

Synthesis



Isopropylamine ↓ $NH_2CH(CH_3)_2$



propranolol.

Mechanism of action

Propranolol is a competitive antagonist of β_1 – adrenergic receptor in the heart. It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart. Blockage of neurotransmitter binding to β_1-receptors on Cardiac myocyte inhibits activation of adenylate cyclase, inhibits cAMP synthesis leading to reduced PKA production. This results in less calcium influx to cardiac myocyte through L-type Ca^{2+} channels, resulting in slowed heart rate, lower blood Arterial blood pressure and Antihypertensive effect

uses 1. treatment of hypertension

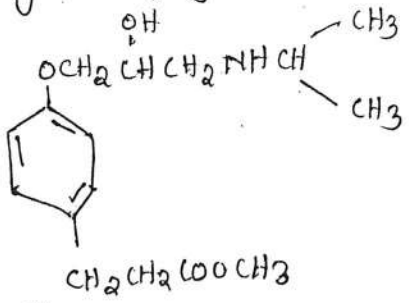
2. Prevention of Acute myocardial infarction and cardiac Arrythmias

Medical uses

oral; for the management of hypertension

ophthalmic: for the management of glaucoma

Atenolol

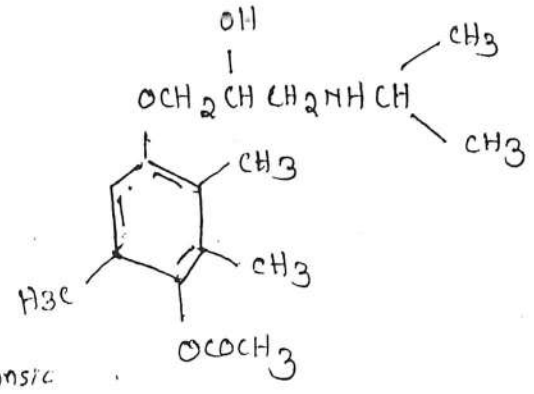


- β_1 – Selective antagonist
- Lacks Intrinsic sympatho mimetic activity and membrane stabilising properties.

Mechanism of action – Atenolol competes with sympathomimetic neurotransmitters such as catecholamines for binding at β_1-adrenergic Receptors in the heart and Vascular Smooth muscle, inhibiting sympathetic stimulation. This results in resting heart rate, cardiac output, and reflex orthostatic hypotension.

uses
1. Management of hypertension and angina pectoris
2. Emergency treatment of cardiac arrythmias.
3. Management of symptoms of Alcohol withdrawal

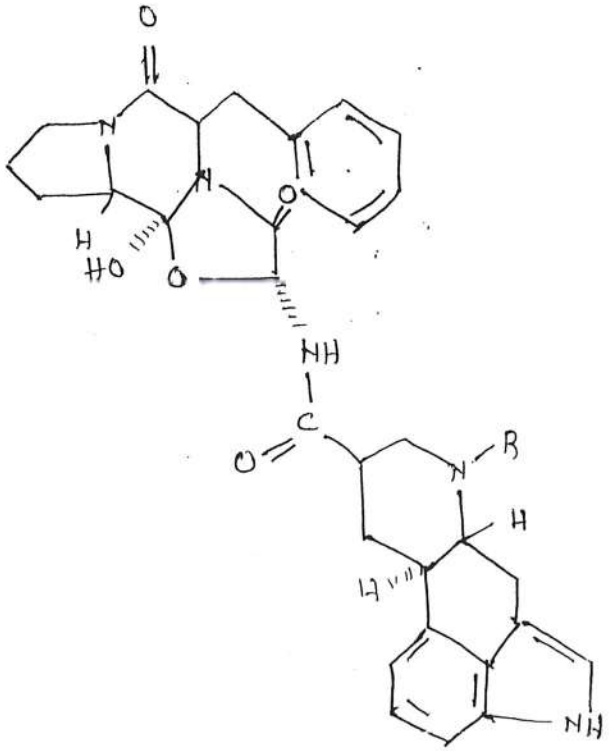
Metipranolol



- Non Cardioselective Beta blocker.
- It lacks Intrinsic Sympathomimetic activity and membrane stabilising properties

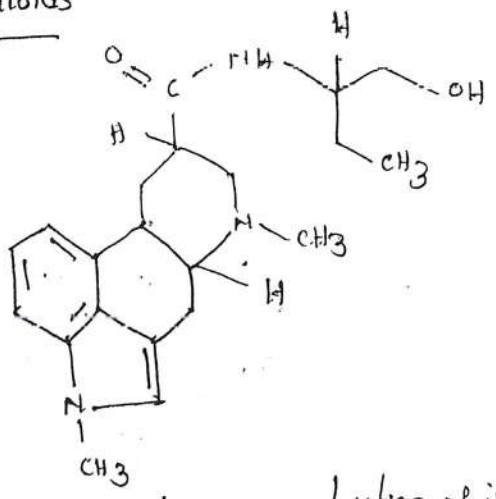
Mechanism of action: Non Selective Beta blockers such as metipranolol, block Sympathetic stimulation mediated by the β_1-adrenergic receptors in the heart and Vasular Smooth muscle, and the β_2-Receptors in Bronchial smooth muscle. The Consequences of β_1-Blockade include Reduction in resting and exercise heart rate and Cardiac output, a rise in systemic and diastolic Blood pressure.

Chemical structure



Ergot alkaloids

1. Methysergide



Mechanism of action

Methysergide is Serotonin antagonist acts on CNS, which directly stimulates smooth muscle leading to Vasoconstriction of intracranial Blood vessels

uses prevention of migraine and cluster headache

2. Dihydroergotamine

Mechanism of action — Dihydroergotamine binds with high affinity to ~~Serotonin~~ $5HT_{1D}a$ and $5HT_{1D}b$ receptors. It also binds with high affinity to serotonin $5HT_{1A}$, $5HT_{2A}$ and $5HT_{2C}$ Receptors.

- Two Theories have been proposed to explain the efficacy of 5-HT_{1D} Receptor agonists in migraine

1. Activation of 5-HT_{1D} Receptor located on intracranial blood vessels, leads to Vasoconstriction with relief of migraine headache.
2. Activation of 5-HT_{1D} Receptors on sensory nerve endings of the trigeminal system results in inhibition of pro-inflammatory neuropeptide release.

uses
(1) Treatment of migraine
(2) Treatment of medication overdose headache
(3) post operative deep vein thrombosis

Muscuranic Receptors are of five types

1. M_1 — present in autonomic ganglia, gastric gland and in CNS. It causes depolarisati histamine release, acid secretion, Affects learning, memory and motor functi

2. M_2 — present in the heart. It decreases velocity of conduction and also loses the strength of contractility.

3. M_3 — present in smooth muscles of the blood vessels and lungs. It causes contracti of smooth muscles and releases NO (nitrous oxide) to produce vasodilatation

4 M_4 - present in the CNS and heart and has no significant clinical effect It may have direct regulatory action on K^+ and Ca^{2+} channels.

5. M_5 - present in the CNS and no clinical effect produced by this receptor It may regulate dopamine release.

Nicotinic Receptors

Nicotinic Receptors derived their name from nicotine, which does not stimulate the nicotinic Receptors but selectively binds to the Receptor

— These are pentameric in structure which encloses a ligand gated cation channel and their activation causes depolarisation and generation of action potential

— Nicotinic Receptors are of two type

(1) Muscle type Nicotinic Receptors (NM) — located in skeletal Neuromuscular junction

(2) Neuronal type nicotinic receptors (Nn) — located in Adrenal medullary ~~cells~~ cells, in spinal cord, in ganglionic cells and in certain areas of brain

Parasympathomimetic agents

These are the drugs / compounds which mimics the actions of Acetylcholine, which is the major neurotransmitter ie causes nerve stimulation.

Classification

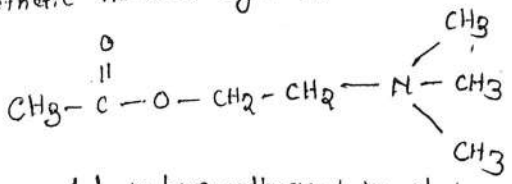
Release of Ach — Release of Ach from storage vesicles is initiated by Action potential that has travelled down to axon

PARA – SYMPATHOMIMETIC DRUGS UNIT – III

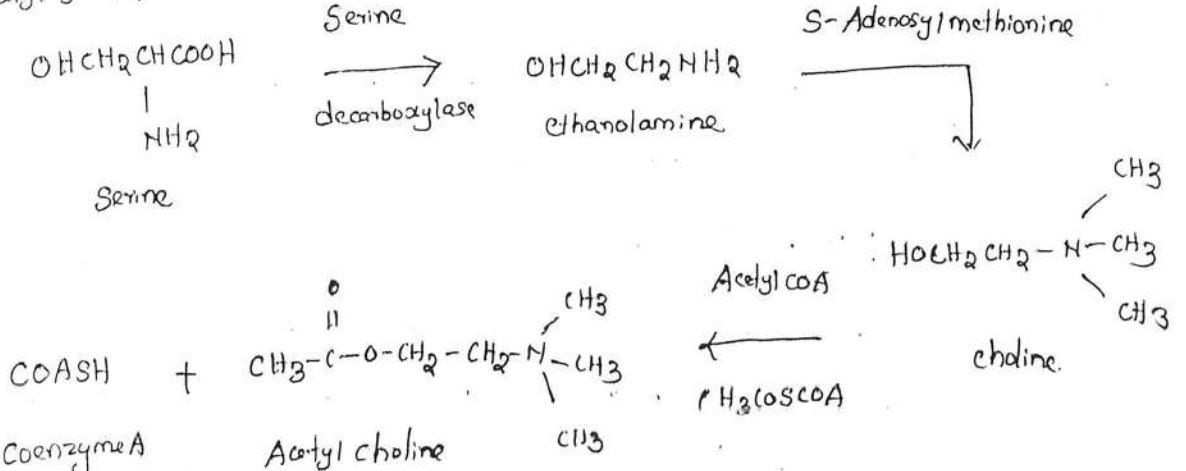
Parasympathetic Nervous system is also known as cholinergic system

Cholinergic neurotransmitters

Acetylcholine is a neurotransmitter which propagates impulse transmission in the parasympathetic nervous system.

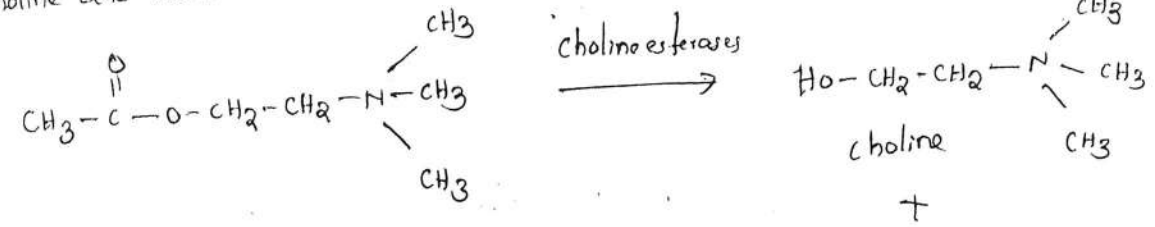


Biosynthesis — Ach is biosynthesised in cholinergic neuron by enzyme-catalysed transfer of acetyl group from acetyl CoA to choline (Quarternary ammonium alcohol) which is biosynthesised from amino acid serine



* Choline is synthesised in the liver by the reaction between serine and ethanolamine.

Catabolism of Acetylcholine — Choline esterases rapidly hydrolyses Acetylcholine into choline and acetic acid.



Cholinergic Receptors

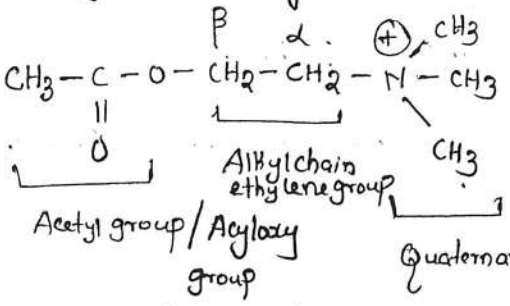
There receptors are broadly classified into

(1) Muscuranic Receptors (M-Receptors)

(2) Nicotinic receptors (N-Receptors)

Storage of Ach – Mostly newly synthesised Ach is actively transported into cytosolic storage vesicles located in presynaptic nerve endings where it is maintained with ATP along with Ca & Mg ions until it is released. only stored form of Ach serves as functional

Acetylcholine is the prototype drug in the category of directly acting parasympatho mimetics. This drug gets rapidly hydrolysed by the enzyme acetylcholine esterases.



A large number of modifications has been made to synthesise new derivatives which are more selective and have longer duration of action.

Modification of the Quarternary Ammonium group

* When the Nitrogen atom of Quarternary ammonium group was replaced with Aresenic, phosphorous / sulphur, though they exhibited little activity of Ach, but these Compounds are less active and not used clinically. It was concluded that only compounds possessing a positive charge on the atom in the position of Nitrogen had appreciable muscaranic activity.
* Compounds in which all three methyl groups on the Nitrogen are replaced by larger alkyl groups are inactive as agonists. When the methyl groups are replaced by three ethyl groups, the resulting compound is a cholinergic antagonist.
* Replacement of one methyl group by an ethyl / propyl group gives a compound that is less active than Ach / lesser muscaranic activity

Modification of the ethylene Bridge

* Replacement of the hydrogen atoms of the ethylene bridge by alkyl groups larger than methyl group affords Compounds that are less active than Ach.
  - Introduction of the methyl group on the β-carbon forms Acetyl β-methacholine (methacholine) which as muscaranic potency almost equivalent to that of Ach and much greater muscaranic than nicotinic selectivity

I. Directly acting agents

A. Choline esters Ex:- Acetylcholine
Methacholine
1 Carbachol, Bethnachol

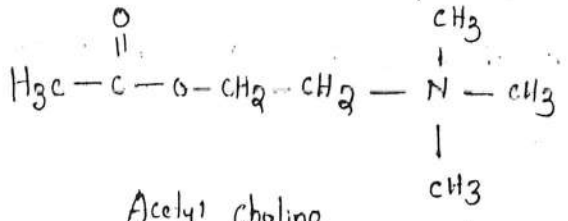
B Cholinomimetic alkaloids – pilocarpine, muscarine, Arecholine

II Indirectly acting agents

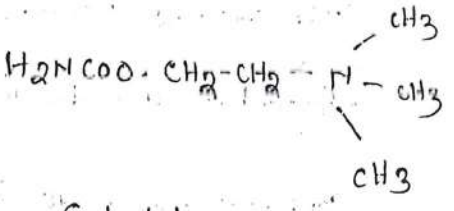
A Reversible cholinesterase Inhibitors – physostigmine, Neostigmine bromide;
Direct acting Pyridostigmine bromide, edrophonium chloride
Ambenonium chloride.

B Irreversible Indirect acting cholinesterase
Inhibitors – parathion, Malathion, Dichlorofenthion etc

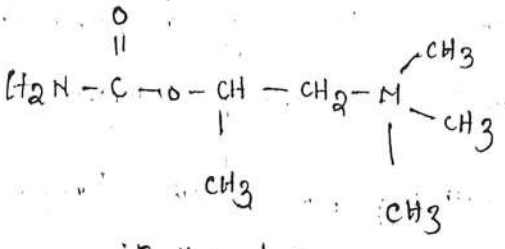
III Cholinesterase Reactivator – pralidoxime chloride.



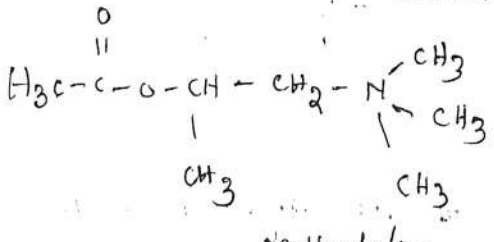
Acetyl choline



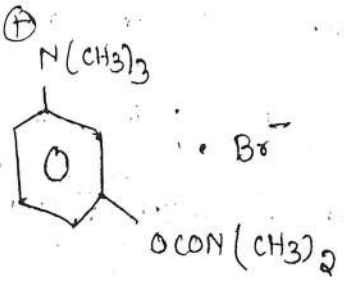
Carbachol

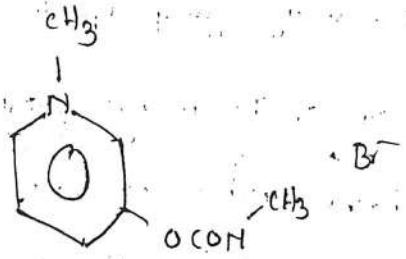


Bethanechol

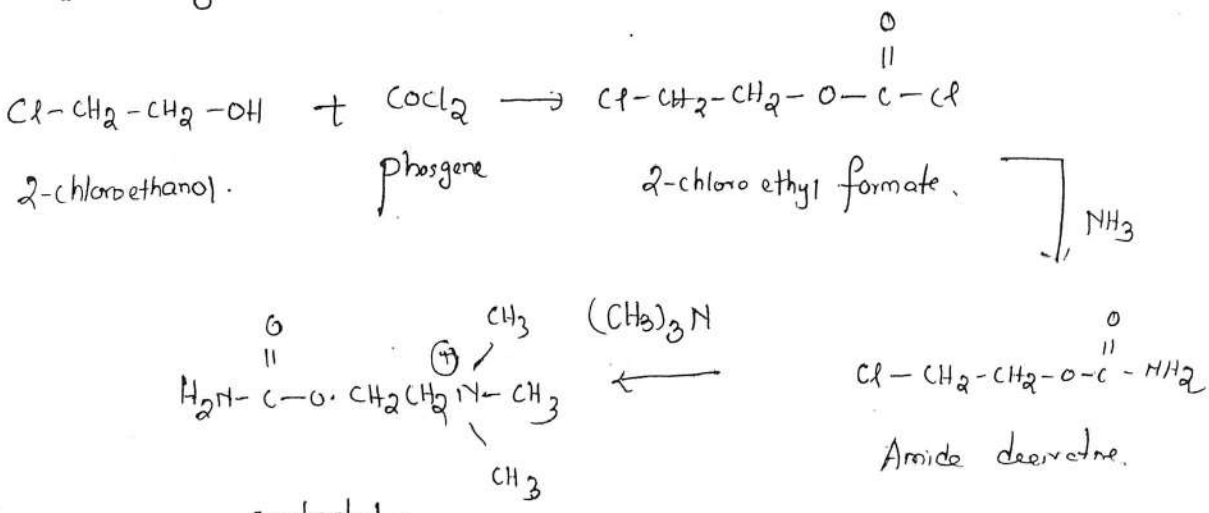


Methacholine

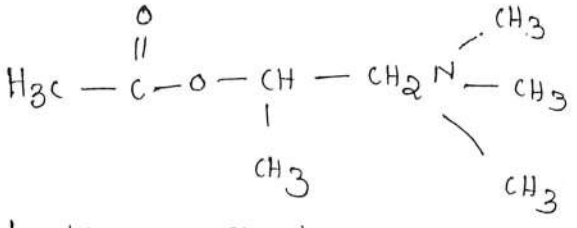




turns into corresponding amide, which is further reacted with equimolar quantity of trimethyl amine gives Carbachol



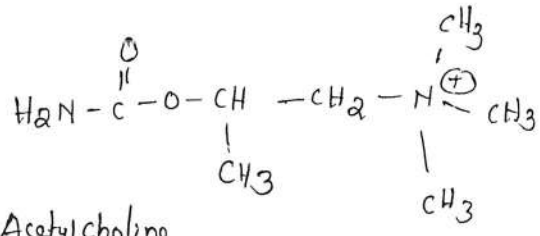
Methacholine



- Selective to Muscuranic Receptors
- Hydrolysed by Acetyl choline esterase enzyme
- MoA — Methacholine acts as a non-selective muscuranic receptor agonist to stimulate parasympathetic nervous system. It is most commonly used for diagnosing Bronchial hyperactivity, using bronchial challenge test. Through this test the drug causes broncho constriction and people with pre-existing airway hyperactivity such as asthmatics, will react to lower dose of drug. Broncho spasm Dyspnoea.

ADR sweating salivation Abdominal pain Nausea

Bethanechol



Not hydrolysed by Acetylcholine esterases

S. Selective to muscuranic Receptors

Uses: Stimulate atonic bladder particularly in post partum or postoperative

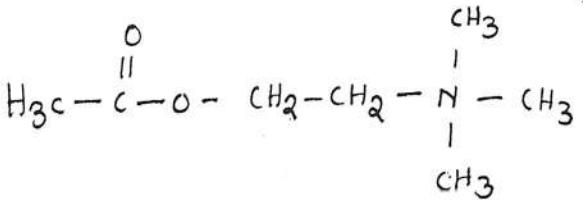
- Smooth muscles of the Bladder & GI tract
- ↑ses intestinal motility and tone
- stimulates the detrusor muscles of urinary bladder causing micturition

1hr dOA

Acetyl choline — Quartenary Ammonium compound

— lacks therapeutic importance

Structure



Chemical Name — 2 - Acetoxy - N,N - trimethyl ethaaminium chloride

Drawbacks — Cannot diffuse through the membrane and Rapidly inactivated.

— It is easily hydrolysed in the presence of choline esterases to form choline and Acetic acid. Hence shorter duration of action.

Parasympathomimetic actions — Ach binds to Muscuronic and Nicotinic Receptors

(1) Rise in Heart rate & cardiac output (-ve chronotropy)

(2) " " B.P

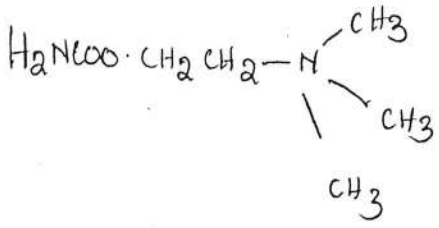
(3) ↑ses Secretions and motility in the GIT (salivary secretions)

(4) Broncho constriction and ↑se Bronchial secretions.

(5) Contraction of Detrusor muscles and urination (urinary Bladder)

(6) Miosis — Contraction of Ciliary muscles.

CABACHOL



— Not hydrolysed by Acetyl choline choline esterases.

— It has Muscuronic & Nicotonic action

— longer duration of action

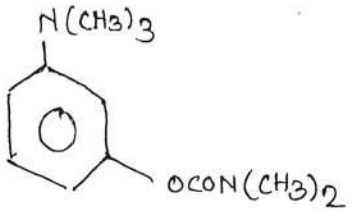
— used as miotic agent in the

— treatment of glaucoma

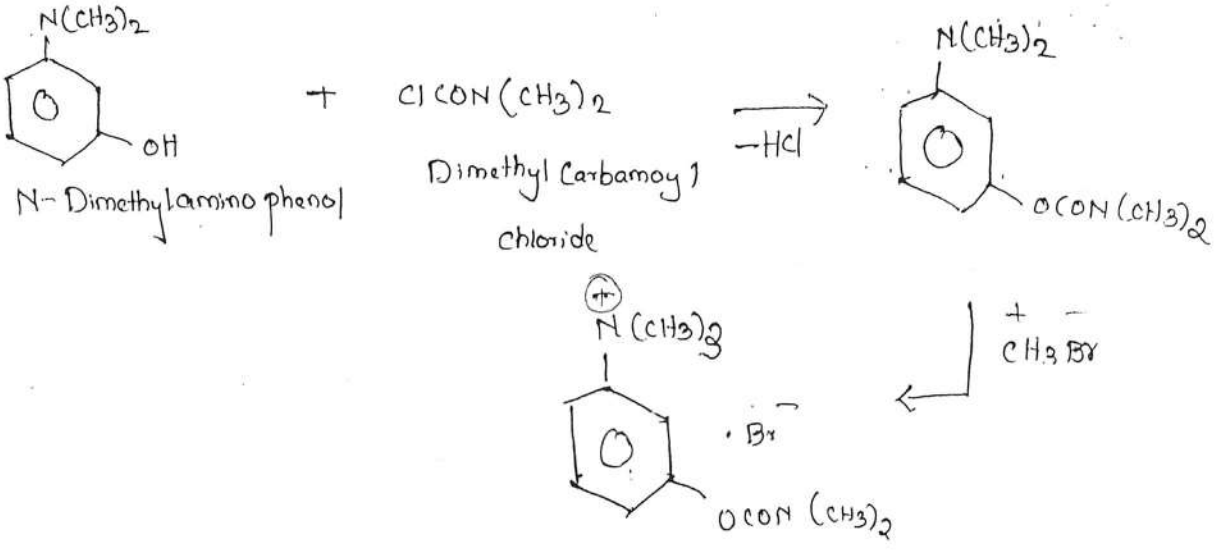
Synthesis — It is made by reacting 2-chloroethanol with phosgene which forms 2-chloroethyl chloro formate upon reaction with ammonia, it

Reversible Inhibitor of enzyme Acetyl choline esterase, responsible for breakdown of Ach in the synaptic cleft of Neuromuscular junction. It indirectly stimulates both nicotinic and muscuranic Ach Receptors.

2. Neostigmine



Synthesis

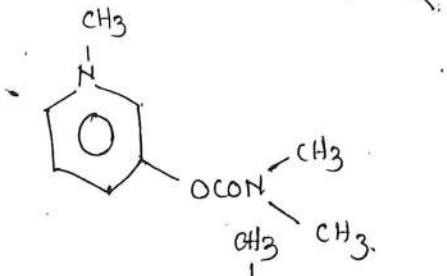


N- Dimethylamino phenol

Neostigmine Bromide

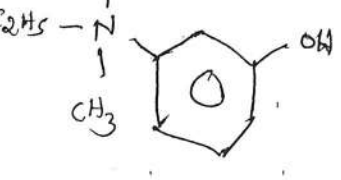
Uses — Treatment of Myasthenia gravis (Skeletal muscle weakness)
- most commonly affected muscles are eyes, face, swallowing
- Urinary Retention problems
- Ogilvie syndrome — acute dilation of Colon (megacolon)

3. Pyridostigmine



Uses — Myasthenia gravis
- Orthostatic hypotension
- Tachycardia

4. Edrophonium



Uses — Myasthenia gravis
- Snake Bites.

Indirectly acting Choline esterase Inhibitors

— These agents are also known as acetyl choline esterase Inhibitors. Acetylcholine esterase is an enzyme which terminates the actions of acetyl choline at the Junctions of various cholinergic nerve endings. These drugs inhibit the AchE enzyme and causes accumulation of Ach in the viscinity of cholinergic nerve terminals. Thus higher concentration of neurotransmitter increases the biological response. These agent thus produce effects similar to that of cholinergic agent

— Anti choline esterase agents are of two types

a) Reversible Inhibitors

b) Irreversible Inhibitors

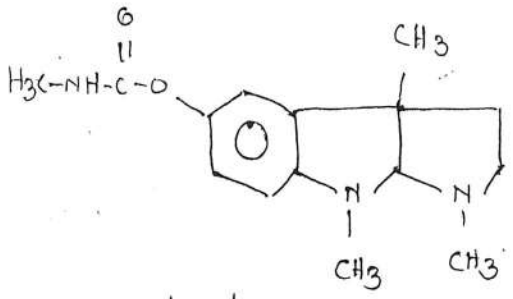
Reversible Inhibitors — As the name indicates, these drugs binds reversibly to the choline subsite. These drugs causes acylation of the hydroxyl group of the Serine residue of acetyl choline esterase. These agent also form an ester like Carbonate / phosphate and covalently binds to the active site of the enzyme

Eg physostigmine, Neostigmine

Irreversible Inhibitors — These drugs produces irreversible inactivation of the acetyl choline esterase. This category includes various organophosphorous Compounds.

Eg parathion, Malathion.

Physostigmine



— Can cross Blood brain Barrier.

— It has miotic function. causing pupillary constriction useful in treating mydriasis.

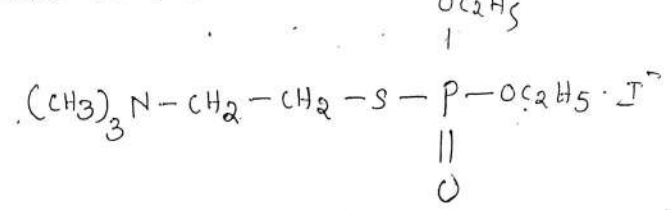
Medical uses — used to treat glaucoma and delayed gastric emptying

— Antidote for choice for Datura stramonium poisoning

— " " Atropine poisoning

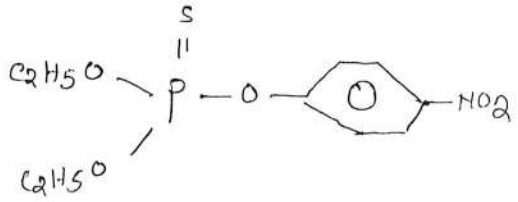
— " " Gamma hydroxy butyrate poisoning

8 Ecothiophate Iodide



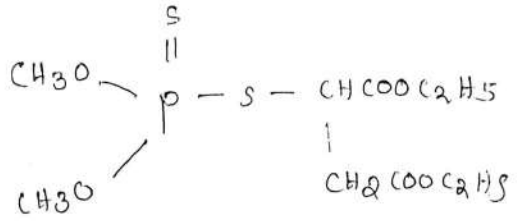
— It is an ocular Antihypertensive in the treatment of chronic glaucoma

9 Parathion / Folidol



— organophosphorous insecticide and pesticide.

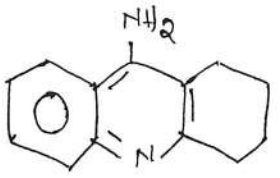
10 Malathion



M.OA Malathion is an acetyl choline esterase inhibitor, a diverse family of of chemicals. upon uptake into the target organism, it binds Irreversibly to several sardom serine residues on the choline esterase enzyme. The resultant phospho ester group is strongly bound to the cholinesterase and irreversibly deactivate the enzyme which leads to rapid build-up of Ach at the synapse-

— organophorous pesticide.

Tacrine Hydrochloride

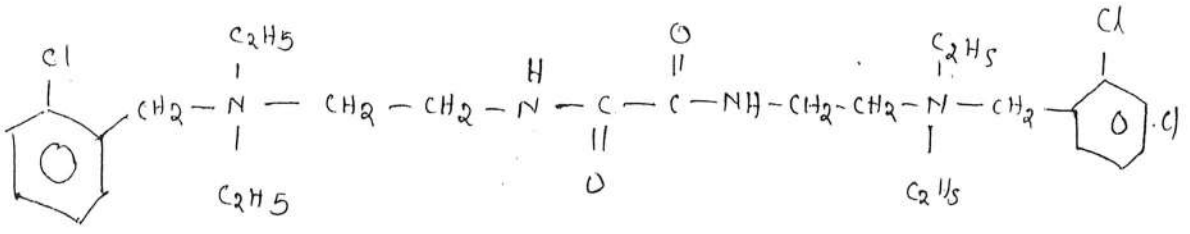


· Hcl.

Uses – First centrally acting choline esterase Inhibitor approved for treatment of Alzheimers disease

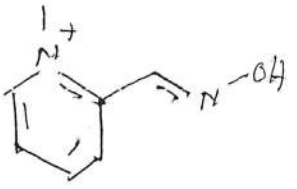
– CNS stimulant effects.

6. Ambenonium chloride

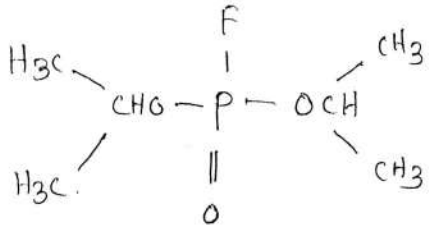


– Management of Myasthenia gravis

Pralidoxime — choline esterase Reactivator —



7. Isoflurophate – Diisopropyl fluro phosphate



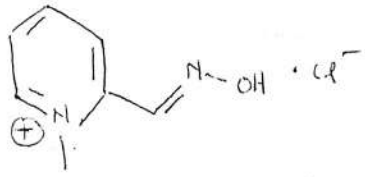
– used in ophthamology as a miotic agent in the treatment of chronic glaucoma.

– organophosphorous insecticide.

Classification

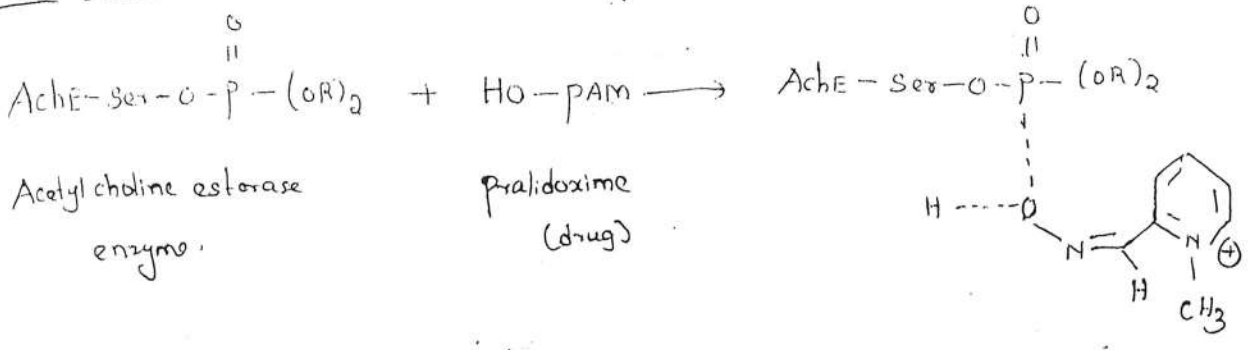
- Antimuscuranic drugs
  - Natural
    - (i) Atropine
    - (ii) Scopolamine
  - Synthetic
    - Structural analogue of Atropine
      - Tertiary ammonium compounds
        - (i) Homatropine
      - Quaternary ammonium compounds
        - (i) Ipratropium
        - (ii) Tiotropium
        - (iii) Atropine methyl nitrate
        - (iv) Homatropine methyl bromide
    - Structurally nonrelated to Atropine
      - Tertiary amines
        - (i) Prenzepine
        - (ii) Dicyclomine
        - (iii) Cyclopentolate
        - (iv) Oxyphencyclimine
        - (v) Tropicamide
      - Quarternary amines
        - (i) Methantheline
        - (ii) propantheline
        - (iii) Isopropamide
        - (iv) Glycopyrrolate

Antidotes for Irreversible Acetylcholinesterase Inhibitors



Pralidoxime Chloride (2-PAM, 2-pyridine aldoxime methyl chloride)

Mechanism of action



Acetylcholine esterase enzyme.

Pralidoxime (drug)

The initial step involves binding of the Quaternary ammonium nitrogen of 2-PAM to the anionic binding site of phosphorylated AchE. This places the Nucleophilic oxygen of 2-PAM in close proximity to the electrophilic phosphorous atom.

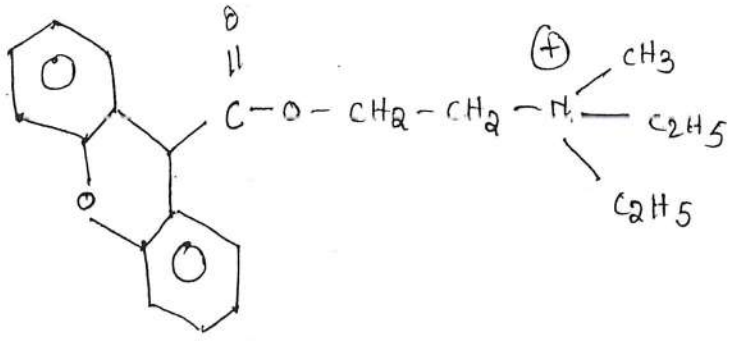
Nucleophilic attack of oxime oxygen results in breaking of ester bond between the Serine oxygen atom and the phosphorous atom. The final products of the reaction are regenerated active form of AchE and phosphorylated 2-PAM. Hence Pralidoxime is known as cholinesterase reactivator.

Uses: It is an Antidote to treat poisoning by a chemical or pesticide or by a drug used to treat a muscle disorder

Cholinergic Blocking agents / Anti-cholinergics / parasympatholytics or Anti spasmodic

units in this chain.

Methantheline Bromide — Synthetic cholinergic drug

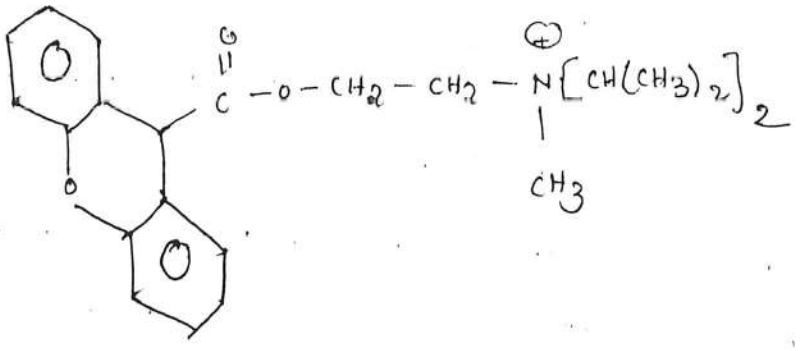


Mechanism of action — Methantheline inhibits the muscuranic actions of Ach on structures innervated by post ganglionic cholinergic nerves as well as on smooth muscles that respond to Ach but lack cholinergic innervation.

Uses — Used to Relieve Cramps / spasm of stomach, intestine & Bladder

— Peptic ulcers

Propantheline



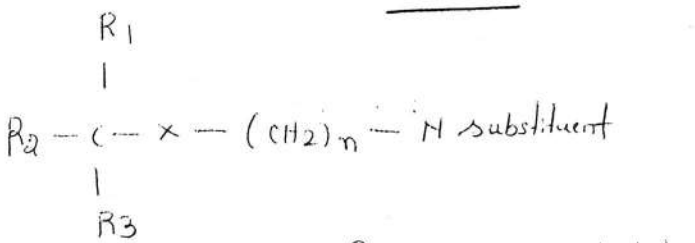
MoA It blocks the actions of Ach, which is produced by nerve cells, to muscuranic receptors present in various smooth muscle tissues such as gut, bladder and eye. Binding of Ach induces involuntary smooth muscular contractions

Use Treatment of spasm of the stomach, intestine & bladder

— treatment of excessive sweating (Hyperhidrosis).

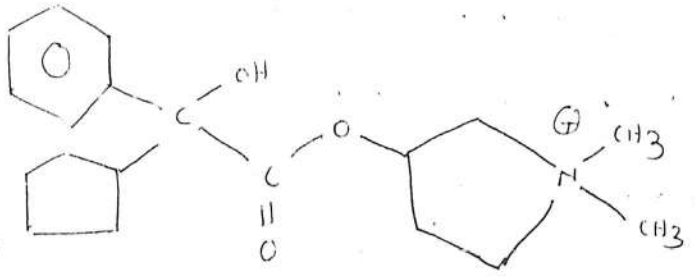
— gastric ulcers.

SAR of Anticholinergic drugs



General framework of anticholinergics

1. The R_1 or R_2 groups must be carbocyclic or heterocyclic, but if both are cyclic it give maximal antagonist potency. The rings may be same or different one is generally aromatic and the other is saturated ring or olefinic group.



Glycopyrrolate.

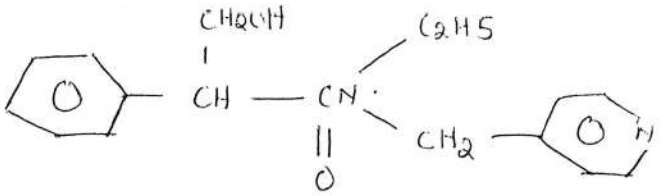
2. The R_3 group can be hydrogen, hydroxyl (–OH), hydroxymethyl (–CH_2OH), amide or a component of R_1 and R_2 group Best potency is seen with hydroxyl or hydroxymethyl this hints that oxygen group must be participating in H-Bond. The hydroxyl group increases binding strength by participating in hydrogen bond interaction at the Receptor.

3. The X Substituent in the most potent anticholinergic agents is an ester, but an ester functional group is not an absolute necessity for muscaranic antagonist activity. This substituent may be an ether oxygen, or it may be absent completely.

4. The N Substituent is a quaternary ammonium salt in the most anticholinergic drugs. This is not a requirement, however because tertiary amines also possess antagonist activity, by binding to the Receptor in the cationic form The alkyl substituents usually are methyl, ethyl, propyl or isopropyl

5. The distance between the ring-substituted carbon and the amine nitrogen

1. Tropicamide



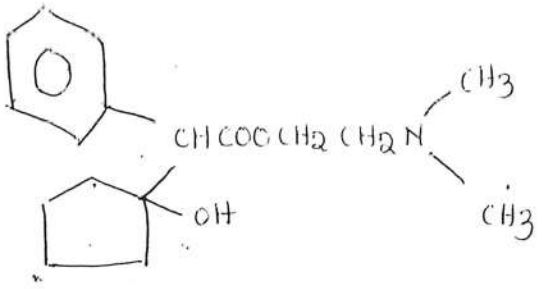
IUPAC Name:- N-ethyl – N – (4-Pyridylmethyl) tropamide.

MOA:- Tropicamide binds to and blocks the Receptors in muscles of the eye (muscuranic receptor M4). It acts by blocking the responses of the iris sphincter muscle to the iris and ciliary muscles to cholinergic stimulation, producing dilation of the pupil (mydriasis) and paralysis of the ciliary muscle (cyclopegia).

uses 1. Short acting mydriatic and cyclopegia when applied as eye drops.

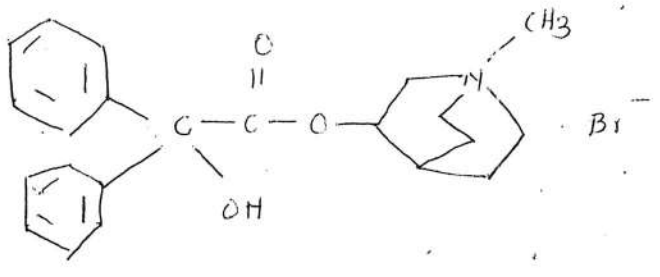
2. used for dilated fundus examinations ~~before and after~~ eye surgery.

2. Cyclopentolate Hydrochloride



uses — used as an eyedrop to produce cyclopegia and mydriasis.

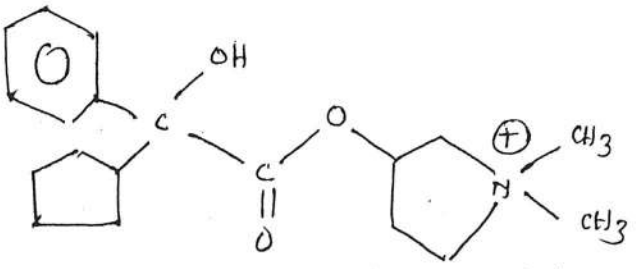
3. Clidinium Bromide — It may help symptoms of cramping and stomach/abdominal pain by decreasing stomach acid.



MOA Clidinium inhibits muscuranic Ach Receptors on smooth muscles, Secretory glands and in the CNS to relax smooth muscle and decrease biliary tract secretions.

Uses:- 1. Prevents the complications of peptic ulcer disease
2. GIT motility disturbances
3. Acute enterocolitis used in fixed combination with Chlordiazepoxide
4. Treatment of Irritable bowel syndrome

4. Glycopyrrolate



— It does not cross Blood-Brain Barrier

MoA — It blocks Muscuranic receptors thus inhibiting cholinergic neurotransmission.

— It loses acid secretion in the stomach and also controls excessive pharangeal, tracheal and Bronchial secretions.

Uses — It is used before surgery to reduce salivary, bronchial & gastric secretion

— Treatment of gastric ulcers.

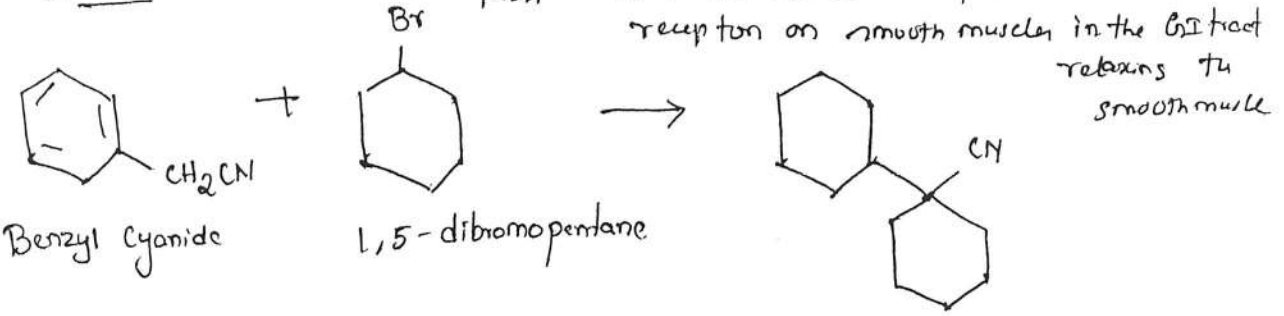
— used to treat chronic obstructive pulmonary disease.

5. Dicyclomine — Uses — Treatment of Irritable bowel syndrome

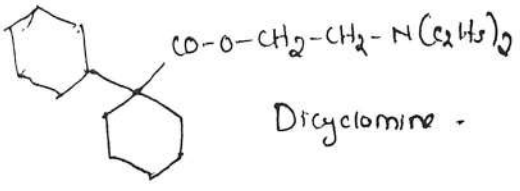
— gastric and duodenal ulcers.

MoA — It blocks the action of Ach on cholinergic receptors on smooth muscles in the GI tract relaxing the smooth muscle

Synthesis

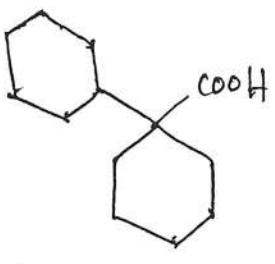


Benzyl Cyanide + 1,5-dibromopentane → 1-cyano-1-phenyl-cyclohexane



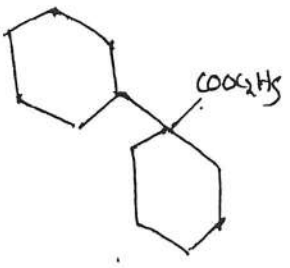
Dicyclomine.

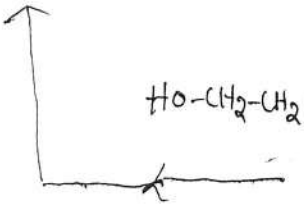
↓ Hydrolysis



Carboxylic acid derivative

esterification ← + C_2H_5OH





2-diethylamino ethanol

MOA:- Biperiden has an atropine-like blocking effect on all peripheral structures which are parasympathetic innervated (e.g.: CVS & Visceral organs)

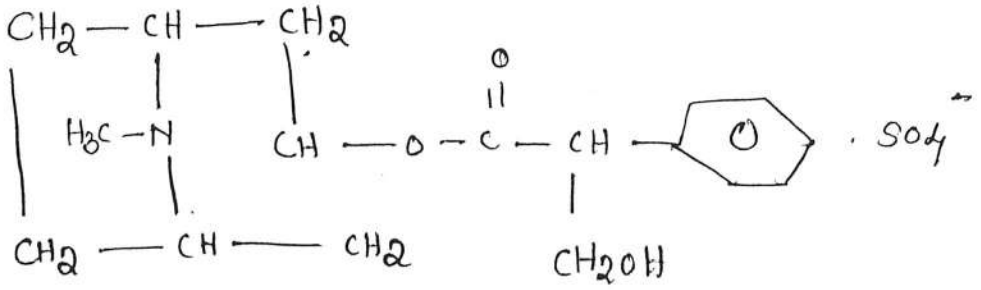
It also has a prominent central blocking effect on M_1 Receptors.

- It is a functional inhibitor of acid sphingomyelinase

Natural Anticholinergic drugs

uses Mydriatic
- Antidote for organophosphon poisoning
- Antispasmodic

Atropine



Mechanism of action - Atropine is a competitive antagonist of muscuranic Ach Receptors ($M_1 - M5$)

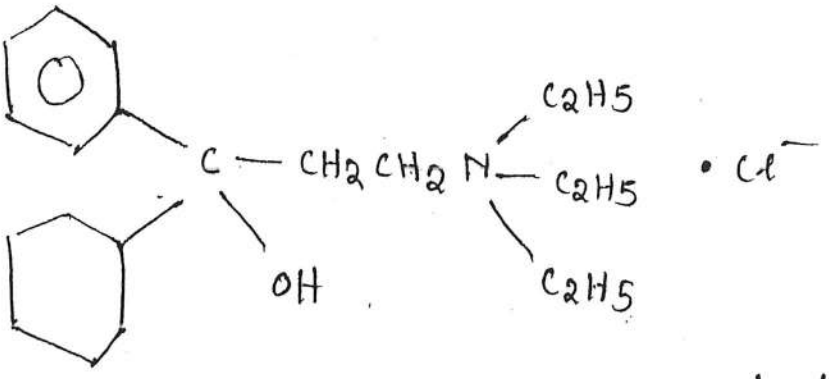
In the eye, atropine induces mydriasis by blocking contraction of the circular pupillary sphincter muscle, which is normally stimulated by Ach release, thereby allowing the Radial iris dilator muscle to contract and dilate the pupil

- Atropine induces cycloplegia by paralysing ciliary muscles, which helps to relieve pain associated with iridocyclitis and treat malignant glaucoma

1. Dilation of pupil
2. ↑ses heartrate
3. ↓ses Secretions (salivary, Bronchial, GI, lacrymal etc)
4. Bladder - It causes urinary Retention and leads Cystitis

D -
U - urination
M -
B -
S -
L -
S -

Tridihexethyl chloride



MOA:- Tridihexethyl binds with muscuranic acetylcholine receptor. It may block all three types of muscuranic receptors including

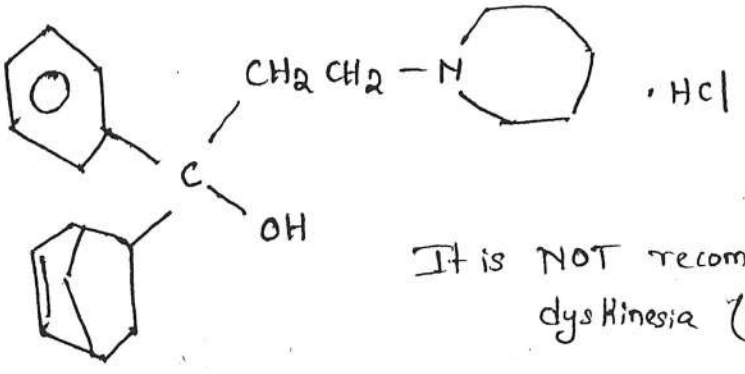
1. M_1 - Receptors in the CNS and the ganglia
2. M_2 - Receptors in the heart.
3. M3 - Receptors at parasympthetic system -

uses:- (1) It is used as antispasmodic and anticulor.

(2) It may be used in combination with other drugs to treat acquired nystagmus (Involuntary eye ball movement / Dancing eyes).

* This drug is discontinued due to unwanted side effect

Biperiden Hydrochloride



It is NOT recommended for tardive dyskinesia (Involuntary Repititive body movement)

uses:- (1) Treatment of parkinsonism and drug induced movement disorde

(2) It Relieves muscle rigidity, Abnormal sweeting and salivation

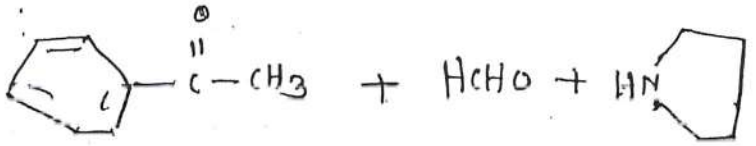
uses 1. Relieves pain due to spasms of voluntary muscle.

2. used in the treatment of parkinsons disease.

3. treat pain arising from Rheumatoid arthritis

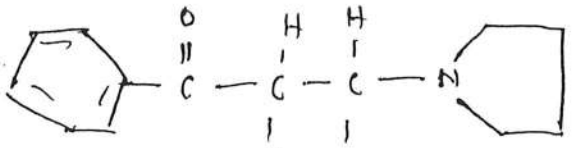
Procyclidine HCl

Synthesis

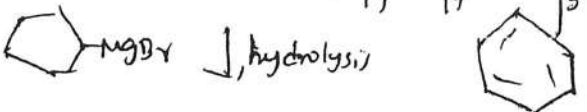


Acetophenone + formaldehyde + 1,3,4,5-Tetra hydro pyrrolidine

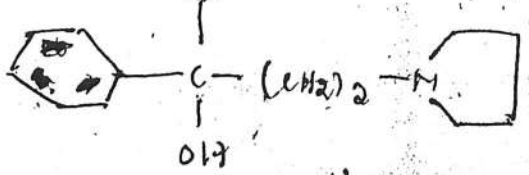
↓ Mannich reaction



β-pyrrolidino propiophenone



↓ hydrolysis

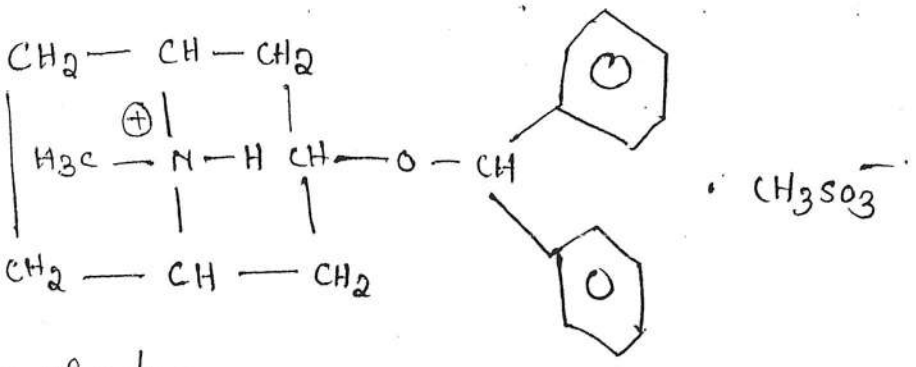


Procyclidine

uses:- (1) Treatment of drug induced parkinsonism

(2) Treatment of movement disorder and acute dystonia

Benztropine mesylate



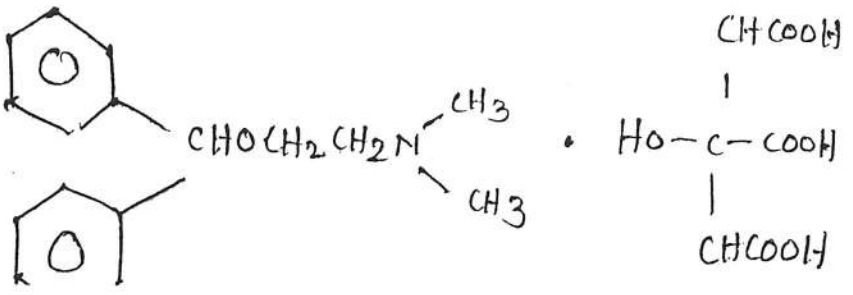
Mechanism of action

Benzatropine is a centrally acting anticholinergic / antihistamine agent. It is a selective M_1 muscuranic acetylcholine receptor antagonist. It partially blocks cholinergic activity in basal ganglia and has also been shown to increase the availability of dopamine by blocking its reuptake and ~~availability~~ storage in central sites, and as a result increasing dopaminergic activity. Its anticholinergic effects have been established as therapeutically significant in the management of parkinsonism. Benzatropine antagonises the effect of Ach, decreasing the imbalance between the neurotransmitters Ach & dopamine which may improve the symptoms of parkinsons disease.

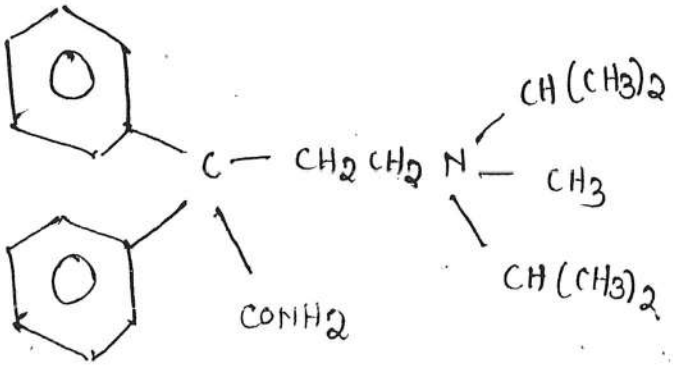
uses

- Treatment of parkinsonism
- Antihistaminic
- Treatment of dystonia (Abnormal muscle contraction)

Orphenadrine citrate



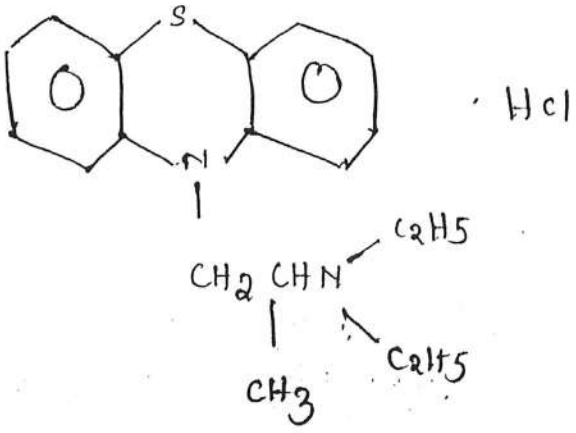
Isopropamide iodide



uses:- long acting anticholinergic drug. It is used in the treatment of peptic ulcers and GI disorders

- treatment of muscular contraction that cause pain, cold - and hyperchlordria -

Ethopropazine Hydrochloride

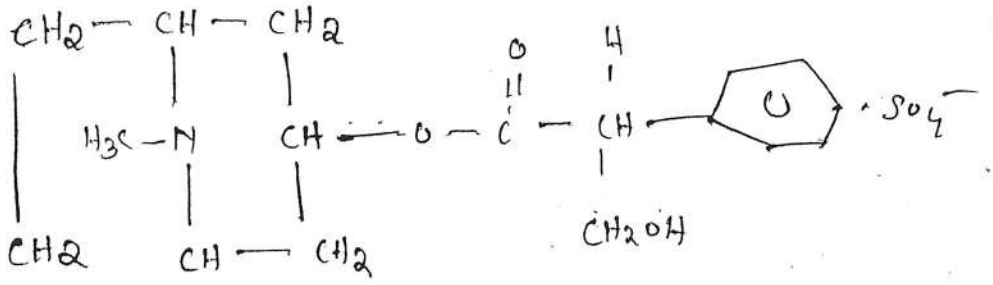


MoA It partially blocks central cholinergic receptor and ~~blocks~~ helps to balance cholinergic and dopaminergic activity in ganglia

Uses Treatment of parkinsonism

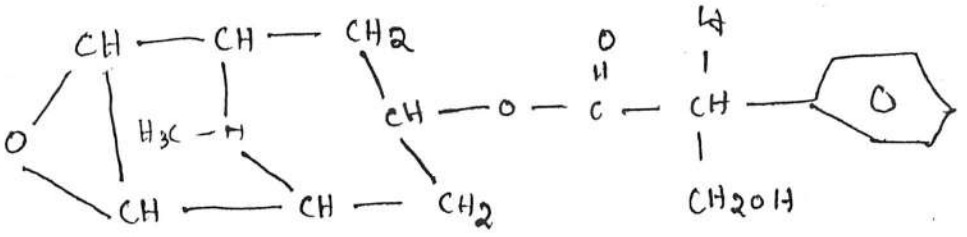
- Antihistaminic properties

Hyoscyamine sulphate



Uses:- Used to prevent motion sickness
- Treatment of parkinsonism
- " " gastric and duodenal ulcer.

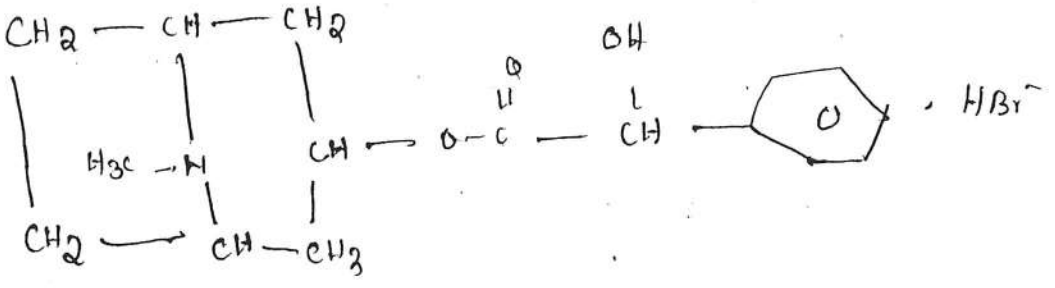
Scopolamine hydrobromide



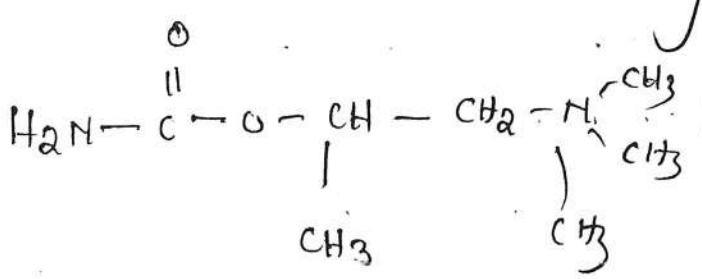
- It is more potent than atropine
- More Rapid onset and shorter duration of action
- More toxic

Uses:- Mydriatic ② Treatment of motion sickness.

Homatropine hydrobromide — Mydriatic

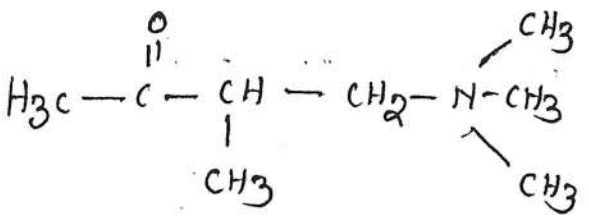


muscarinic agonist with almost no nicotinic activity



Bethanechol

- The ester group of Ach helps in hydrogen bonding formation with the Receptor. If large aromatic groups are inserted into the ester group it will produce Ach Antagonist ie may act as anti-cholinergic drug



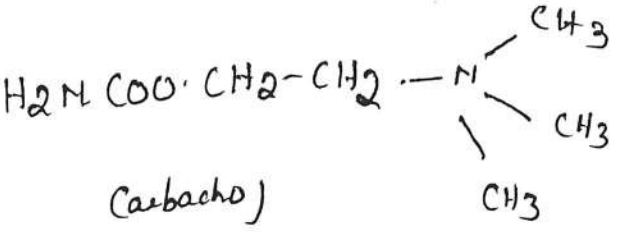
Methacholine

* A methyl group on α-carbon to the Quaternary nitrogen affords Acetyl α-methyl choline. Therapeutic activity is reduced when compared with Ach. at both muscuranic and nicotinic receptors. This compound is not used clinically

Modification of the Acyloxy group

When the Acetyl group is replaced by higher homologues ie the propionyl/ butyryl groups the resulting esters are less potent than Ach

The chemical instability of Ach result from its Rapid hydrolysis, a logical Approach to the development of better therapeutic agents was to Replace the Acetyloxy functional group with a functional group more resistant to hydrolysis. This led to synthesis of the Carbamic ester of choline (Carbachol) a potent cholinergic agonist possessing both muscuranic and nicotinic activity. Esters derived from carbamic acid are referred to as Carbamates, and because their Carbonyl carbon is less electrophilic they are more stable than Carboxylate esters to hydrolysis.



(Carbachol)

Carbachol is less readily hydrolysed by gastric acid, AchE than ach, and can be administered orally.

This chemical logic was extended to methacholine and led to synthesis of its compound Bethanechol, an orally effective potent

Uses:- — Treatment of Asthma

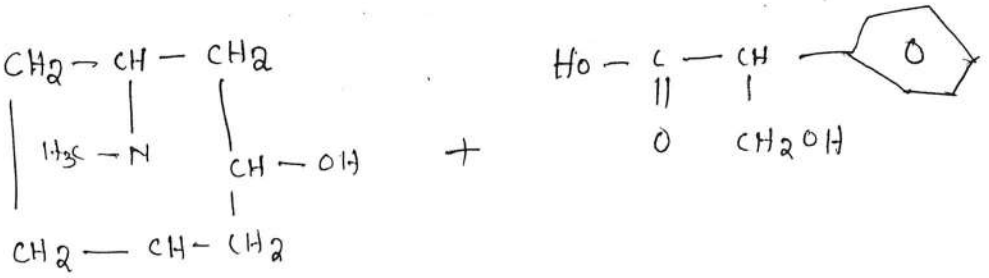
— Treatment of COPD

and constriction and inhibition can lead to bronchodilation and fewer secretions

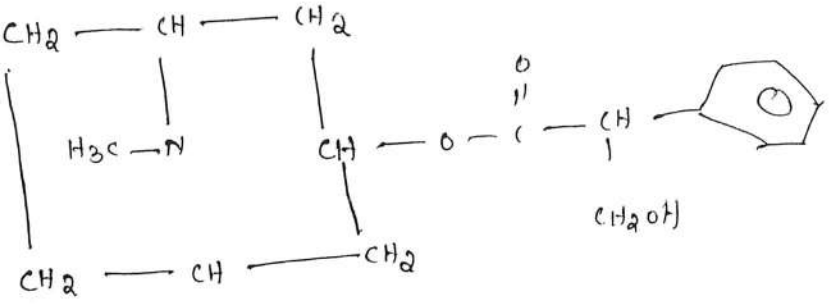
∴ Administration of ipratropium stops the action of Ach on smooth muscle preventing the contraction and relaxation of airways take place.

Ipratropium bromide

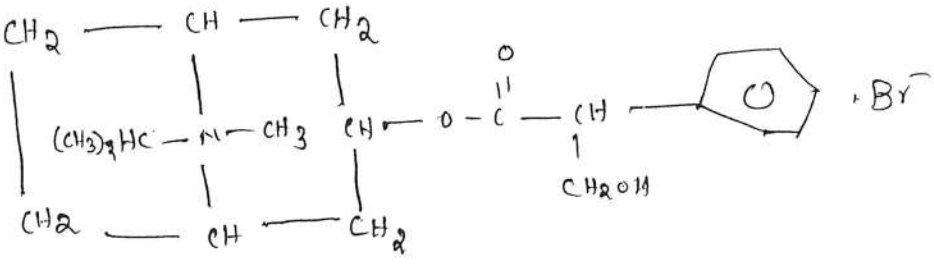
Synthesis



↓ HCl



↓ $(CH_3)_2CHBr$



Ipratropium Bromide

MOA Ipratropium acts as an antagonist of the muscaranic Ach Receptor. This effect produces the inhibition of the parasympathetic nervous system in the airways and hence inhibits their function. The function of the parasympathetic system in the airway is to secrete bronchial secretion

Date
14 | 4 | 2020

Day - Tuesday

UNIT - 4th

Drug Acting on Central Nervous System

Sedative and Hypnotics

Sedative and Hypnotics are those drugs which act on the CNS and they reduce the mental excitement and mental depression depress and produce the Natural sleep and sound sleep.

Sedative | Mental excitement
↓
Dipression
Drowsiness

Hypnotics - Relaxed
Natural sleep
Sound sleep.

Sedative - Sedative are those drug which donot produce sleep but they reduce the excitment of brain ad and depression and produce Drowsiness.

Hypnotics - Hypnotics are those drug which have higher concentration than sedative and they basicly relax brain or complete relax the brain and produce natural sleep or sound sleep.

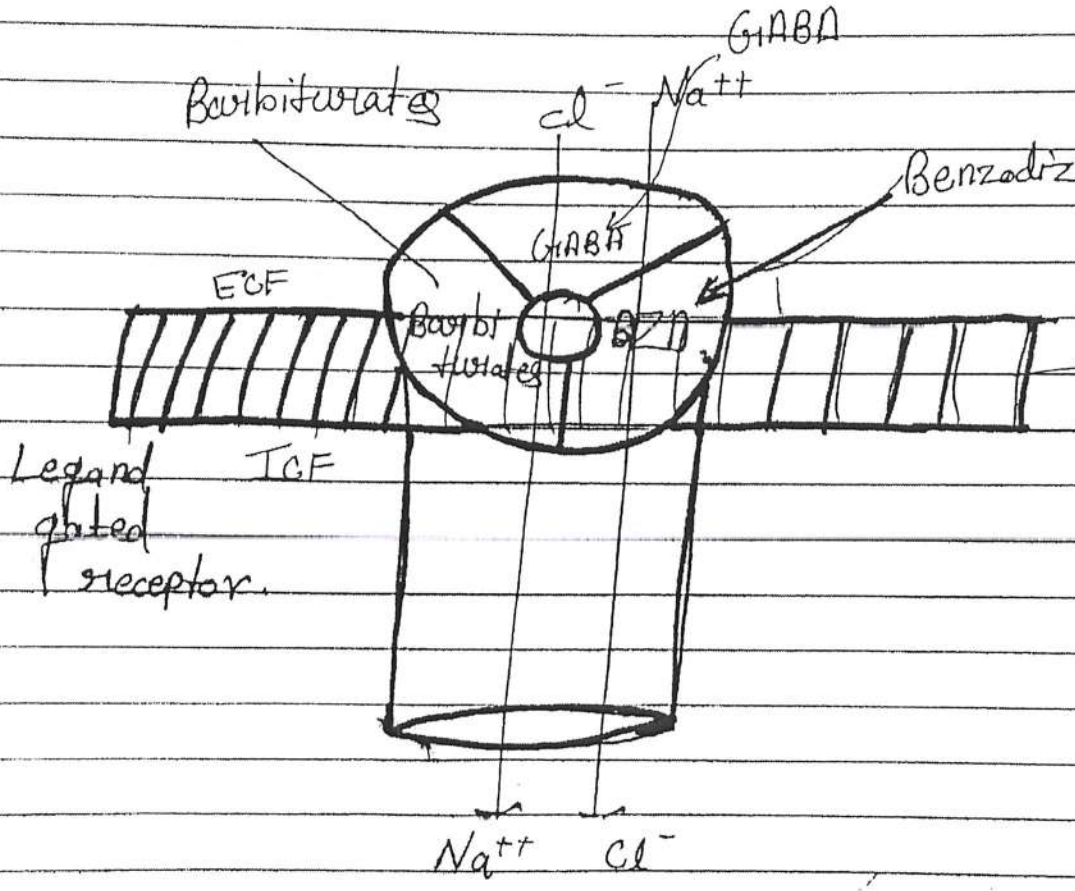
Mode of Action of Sedative and Hypnotics

Basicly sedative and hypnotics drugs are in of 3 category -

- GABA analog
- Benzodizapine
- Barbiturates

- When any of the drug (Barbiturates, Benzodizapine, GABA analog) bind with their selective receptor like benzodizapine bind with Benzodizapine receptor, Barbiturates bind with the barbiturates receptor and these drug bind with the receptor then channels are open and chlorides ions moves from ECF to ICF and chloride ions moves then channel receptor becomes high polorised the transmision of Na^{++} is completly stoped and in that case brain

becomes relax and the excitment of brain is reduced and Sedative and hypnotics action produce in our CNS side



Classification of Sedative and Hypnotics Drugs

1. Barbiturates

Long acting - Phenobarbitone.
Short acting - Butobarbitone
Ultra-short acting - Thiopentane Methohexitone.

Trick - अगर बार्बी को बुलाना है तो कैन बुताओ थपकी दो साथ पर और सख्त तीन से लोरी गाओ।

2. Benzodiazepines Hypnotics

Diazepam
Fluorazepam
Nitrazepam
Triazolam
Temazepam
Alprazolam.

Trick - दिया को फ्लू हो गया था नाइट शो पर दिवाली के तमीज नही रात भर बेंजो पर अलाप गाता रहा।

3. Newer Non benzodiazepine hypnotics.

Zolpidem
Zaleplon
Zopiclone.

Trick - नए लोग जाल बिछाते है पिंड में प्लान के साथ क्लीन बनाते है।

(11) Benzodiazepines -

- Benzodiazepine is an sedative and hypnotics drugs.

They have diazepine ring which is attach with benzene ring.

- Benzodiazepine drugs are available in both ionised and unionised form when hydroxyl (OH) group is attach the benzodiazepine ring then it becomes polar and ionised.

- If Benzodiazepine given in nonionic / unionised form then their absorption and protein binding much very well. if given in ionised form then their duration of action and metabolism is reduce.

- Benzodiapini drug bind with the benzodiazepine receptor and gama (γ) analogue recepter and produce sedative and hypnotics action.

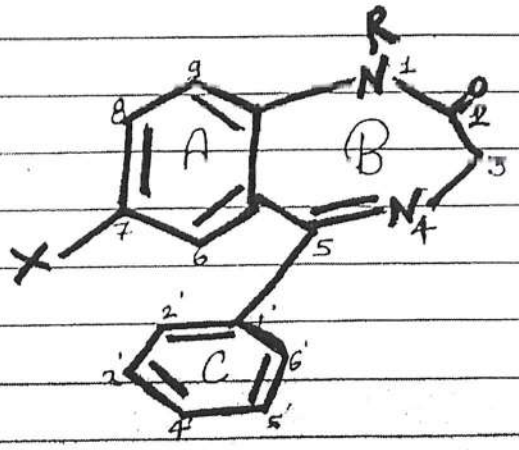
V.V. Imp

SAR of Benzodiazepam

- In the structure of benzodiazepam for the study of SAR, we can devided this molecule into 3 parts -

Ring A - Aryl / Heteroaryl group
Ring B - 1,4 Benzodiazepene Group
Ring C - Phenyl substituent.

- Ring A Aryl / Hetroaryl group, Ring B is 1,4 Benzodiazepene group and Ring C is Phenyl substituent. group at position 5.



Benzodiazepene.

[1] Aryl / Hetroaryl Moeity -

- In Aryl / Hetroaryl moiety, there are 3 essential things are important for their activity

- It should be Aryl / Heteroaryl ring.
- It should be aromatic in nature.
- It should be have π - π conjugation.

- At position 7 in ring A electronegative atom is essential and more electronegative atom will be attached the activity will be ↑es multiple numbers of ~~ty~~ times.

Ex. NO_2, F, -Cl, -Br, -I, $-SO_4$

- In the position of 6, 8 and 9 when we add any functional group or any moiety then the activity of benzodiazepine ring is ↓es.

1.4 Benzodiazepene Group -

- Alkyl substitution at no. 1 nitrogen is essential for activity.
- The ketone group present at position no. 2 is also essential for ~~activity~~ receptor binding activity.
- The double bond b/w 4 and 5 position (nitrogen and Carbon) essential for activity.
- Phenyl substitution at position no. 5 is also essential for activity.

- Alkyl substitution at position no. 1 with Nitrogen atom is essential for activity
  If this nikil substitution is smaller 2, 3 carban their activity will be ↑es.
  If ↑es the chain length the activity of this Benzodiazepen is ↓es.
- At the position no. 3 when add the OH group then there is no change in their activity.
  But due to posining of hydroxyl group there polarity is ↑es so rate of metabolism and rate of excretion is also ↑es and their duration of action is ↓es.
- When we donot add any OH group at position no. 3 then their duration of action is ↑es.

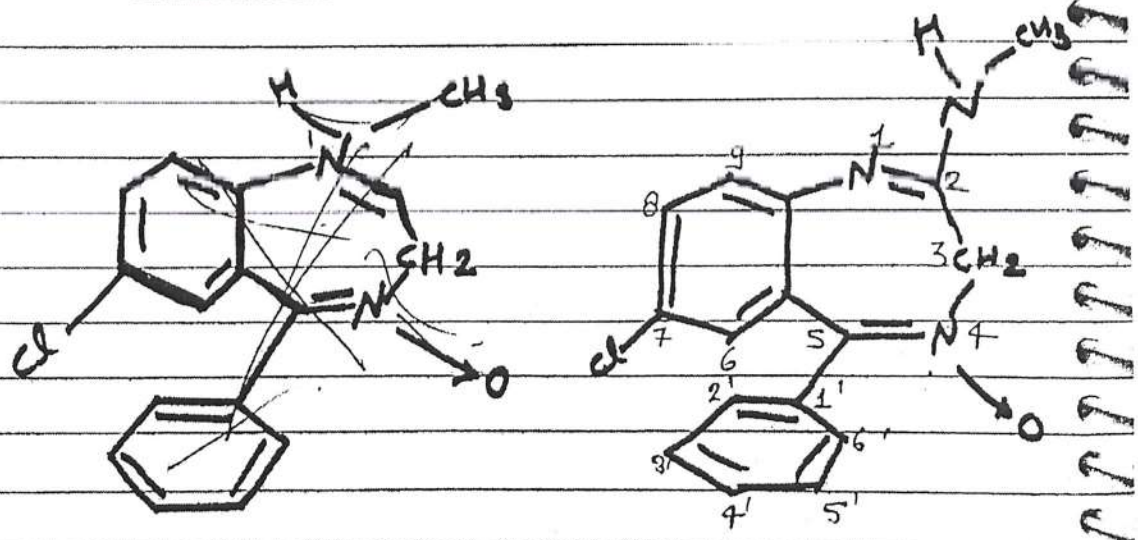
[3] Phenyl Substitution -

- The attachment of ring at 5 position is essential for activity.
- The nature of phenyl group should be arromatic it is essential for activity.
- They should have Pi conjugation.

- When we add any substitution on position 2 and 6' on ~~#~~ ortho position then their activity ↓es.
- When we add any substitution at 4' position or para position then their activity will be ↑es.

Brief Notes on of Benzodiazepine Drugs

[1] Chlordiazepoxide

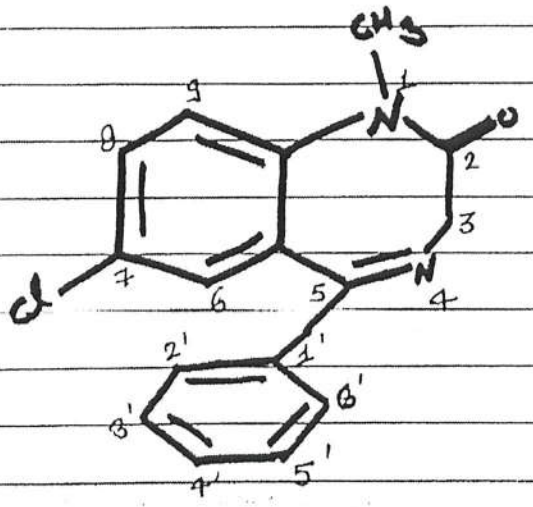


- Chlordiazepoxide is chemically. 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine-4-oxide.
- It is a sedative and hypnotics drug under the benzodiazepine class and the first benzodiazepine to be synthesized.

- It is a long-acting drug and even its metabolite is active and has a long-life.

Uses- • It is used in the management of epilepsy, anxiety, insomnia and alcohol or drug abuse withdrawal symptoms.

Im 21 Diazepam



- Diazepam is chemically, 7-chloro, 1, 3-dihydro-1 methyl-5-phenyl-2H-1,4-benzo-diazepine -2-one.

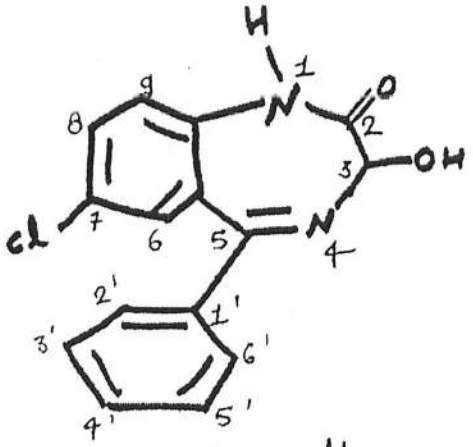
- It is a sedative and hypnotic drug under the benzodiazepine class and produces a calming effect.

- It acts by Tesing the effect of neurotransmitter $GABA_A$ receptor activity leading to CNS depression.

Uses - • Diazepam is most frequently prescribed medications in this world under the class of benzodiazepines.

- It is used in the management of epilepsy, anxiety, insomnia, muscle spasms, seizures, trouble sleeping, restless legs symptoms and alcohal or drug abuse withdrawl symptoms.

[3] Oxazepam

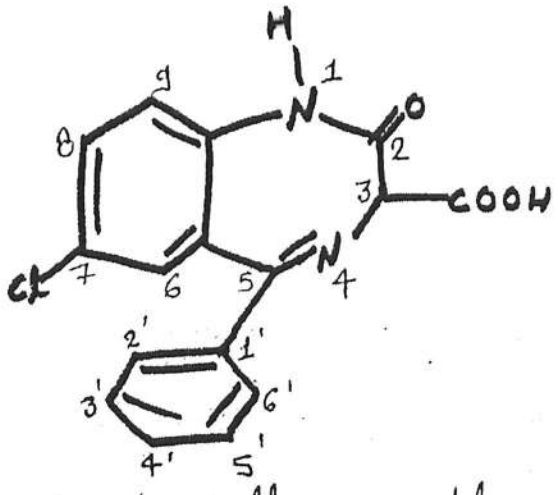


- Oxazepam is chemically, 7- chloro - 1,3 dihydro- 5 - phenyl -2H - 1, 4 - benzo - diazepin - 2 -one.
- Oxazepam acts on benzodiazepine receptors resulting in Tesed effect GABA to $GABA_A$ receptor which results in inhibitory effects on CNS.
- Oxazepam exists as a racemic mixture, and has no therapeutic benefit to administration of a single enantiomer over the racemic mixture.

- It is a short acting benzodiazepine with a slow onset of action.
- It is an example for an active metabolite formed during the metabolism of diazepam and other benzodiazepine drugs.
- It doesnot required hepatic oxidation, and is simpley metabolized by glucoridation. So oxazepam is less likely to accumulate and cause adverse reactions.

Uses - • Oxazepam is used in the management of anxiety, insomnia and in the control of symptoms of alcohal withdrawal syndrome.

[4] clorazepate

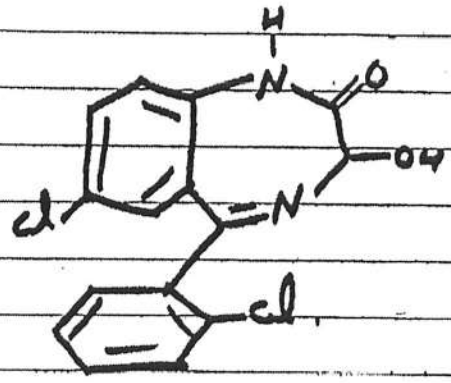


- Clorazepate is chemically, 7 chloro - 2-3- dihydro - 2-oxo - 5- phenyl - 1H-1,4 - benzodiazepine - 3- carboxylic acid.
- It acts on benzodiazepine receptors resulting Tesed effect of GABA to the $GABA_A$ receptor which results in inhibitory effects on CNS.

- Clorazepate is an example for prodrug. the parent drug undergo decarboxylation in the acidic environment of the GIT to form nordiazepam, a non-polar and active metabolite with half-life of more than 40 hours.

Uses:- • It is a long acting benzodiazepine medication, and finds importance as anxiolytic, anticonvulsant, sedative, hypnotic, and skeletal muscle relaxant.

[5] Lorazepam

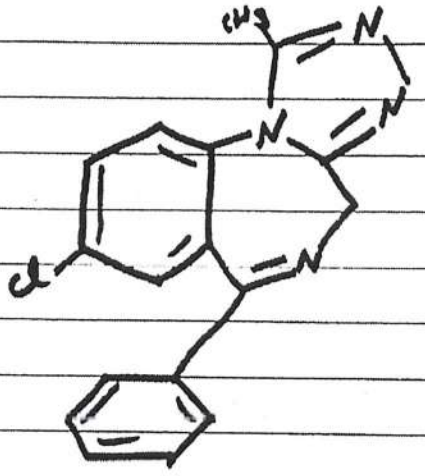


- Lorazepam is chemically, 7-chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-2H-1,4-benzodiazepin-2-one.

- It acts as benzodiazepine receptors, resulting in Tesed effect of GABA to the GABAA receptor which results in inhibitory effects on CNS.

Uses:-
- Lorazepam is benzodiazepine medication, used to treat anxiety, insomnia, seizure and chemotherapy-induced nausea and vomiting.
- It is also finds importance as preoperative medication.

[6] Alprazolam

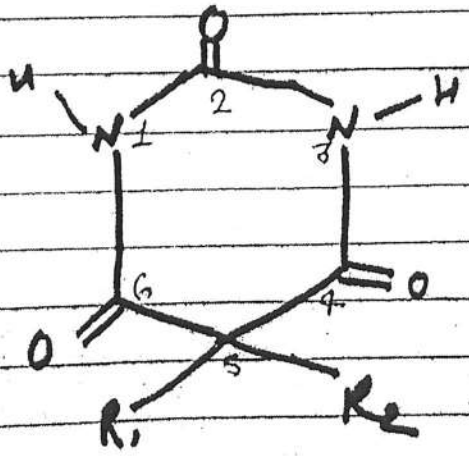


- Alprazolam is chemically, 8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine.
- It acts on benzodiazepine receptors, resulting in potentiated effect of GABA to the GABA$_A$ receptor which results in inhibitory effect on CNS.

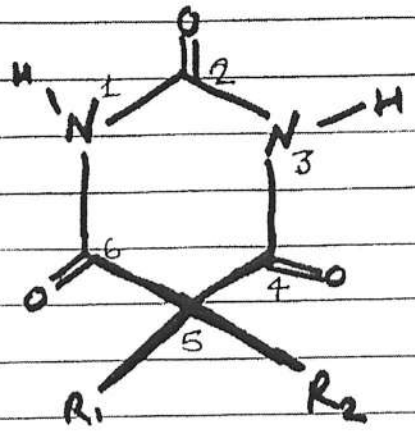
Uses:-
- Alprazolam is a potent, short acting benzodiazepine drug, and finds importance as an anxiolytic, sedative and ~~hypnotic~~ hypnotic.
- It is commonly used for the treatment of generalized anxiety disorders or social anxiety disorder.

2. Barbiturates

- Barbiturates are basicaly sedative and hypnotic drug they bind with the barbiturate related receptor and activate the GABAA receptor and they hyperpolarised the receptor and depress the brain in functioning.
- In the Barbiturates ring basicaly hexahydro pyrimidine ring is present and they contain 3 ketone group and 2 alkyl substitution.
- There chemical name is 5, 5 dialkyl substituted 2, 4, 6 trioxo hexahydropyrimidine.
- As per the ring barbiturates are acidic in nature.

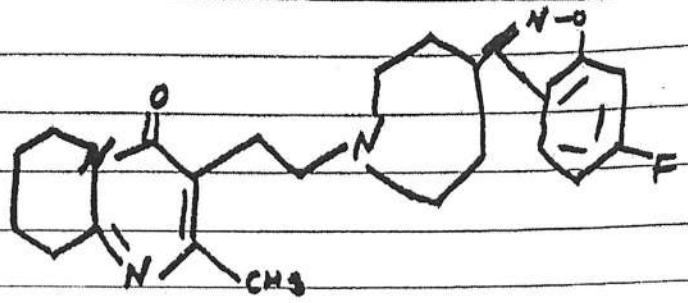


SAR of Barbiturates



- In the barbiturates structure hexahydro pyrimidine ring is essential for activity.
- 3, Oxo group at the position of 2, 4, 6 is essential for activity.
- At the position no. 5, two substitution is essential for the activity.
- When we ~~replace~~ placed the hydrogen atom at both R1 and R2 position in carbon no. 5 then activity will be ↓es.
- At carbon position no. 5 when 1 alkyl alkyl group is replace with alkyl carbon chain and another contains hydrogen atom then activity will ↑es.

3. Risperidone



Risperidone

- Risperidone is a benzisoxazole derivative, chemically it is, 3-[2-(4-(6-fluoro-1,2-~~pyri~~ benzoxazol-3-yl) piperidin-1-yl] ethyl)-2-methyl-6,7,8,9 tetrahydropyridal [1,2-a]-pyrimidine-4-one.

- Risperidone selectively at antagonizes serotonin 5-HT2 receptor.

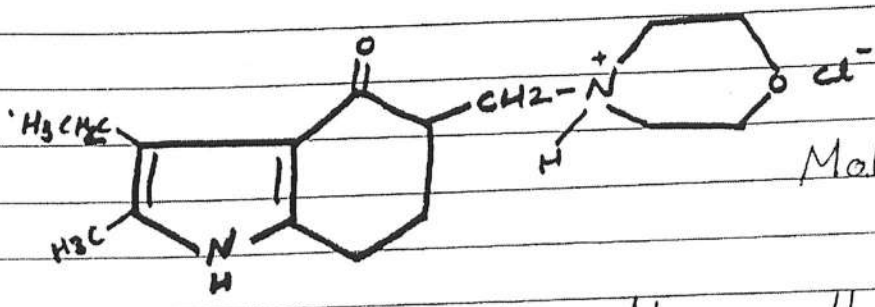
- It also binds with limbic dopamine D2 receptor which leads to antipsychotic activity.

Uses- • Risperidone acts as an atypical antipsychotic agent.

It is reported to treses the negative (eg- withdrawal apathy) as well as the positive (eg- delusions hallucination symptoms of schizophrenia.

Beta Amino Ketones

1. Malidone Hydrochloride



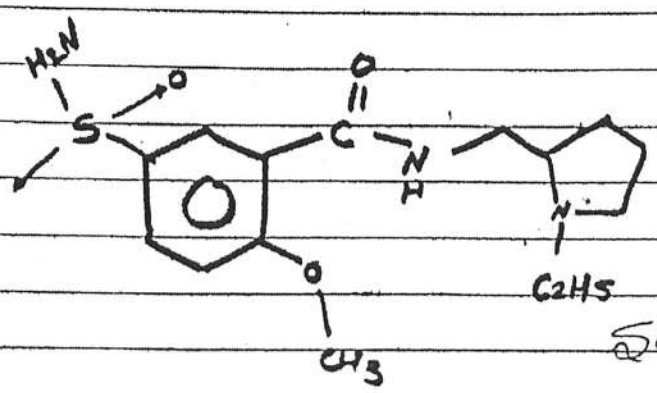
Malidone HCl

- Malidone HCl is chemically 3-ethyl-2-methyl-5-(morpholin-4-ylmethyl)-1,5,6,7-tetrahydroindol-4-one hydrochloride.
- It exerts its effect by blocking dopamine receptors (D_2 and D_3) in the reticular activating and limbic systems, thereby lessing dopamine excess in the brain.
- It also has moderate affinity for cholinergic and alpha-adrenergic receptors.

Uses -
- Malidone is a convential antipsychotic used in the therapy of schizophenia and other psychoses.
- It is useful in the treatment of aggressive type of undersocialized conduct disorder.

Benzamides

1. Sulpiride



Sulpiride.

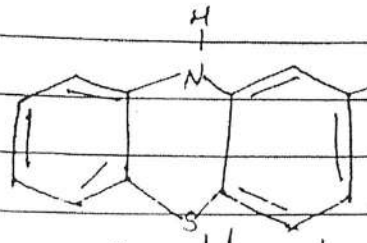
- Sulpiride is benzamide derivative. chemically N-[(1-ethylpyrrolidin-2-yl) methyl]-2-methoxy-5-sulfamoylbenzamide.
- It is more selective and acts primarily as a dopamine D_2 antagonist.

Uses - • Sulpiride is used therapeutically as an antipsychotic.

- It is also used as antidepressant and as a digestive aid.

Synthesis

Chlorpromazine Hydrochloride

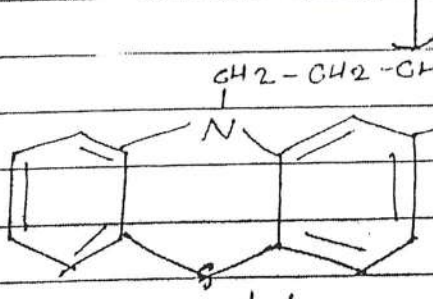


2-chlorophenothiazine

+ Cl-CH2-CH2-CH2-N(CH3)(CH3) . Hal

3-chloropropyldiethylamine hydrochloride.

Reflux | Toluene Sodamine



chlorpromazine hydrochloride.

Day - Wednesday

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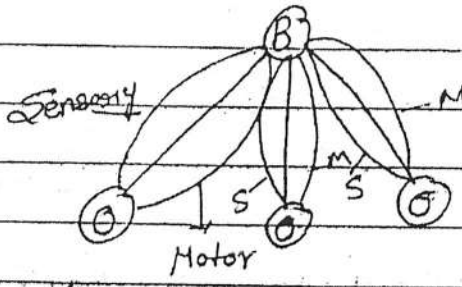
UNIT - 4th

Chapter - 3

Anticonvulsant - Epilepsy / Seizure

- Most commonly seizure is also known as Epilepsy.
- It is derrived from Greek word - Epilambey which means To seize.
- It is an neurological disorder, in which the neurohumaral transmission of the brain is completly affected.



- In epilepsy there is a abnormal sensory and motor numoral discharge so funation of all organ in body or funation of muscles is completly changed and seizures or convulsans are comes out which is called convulsant / epilepsy.

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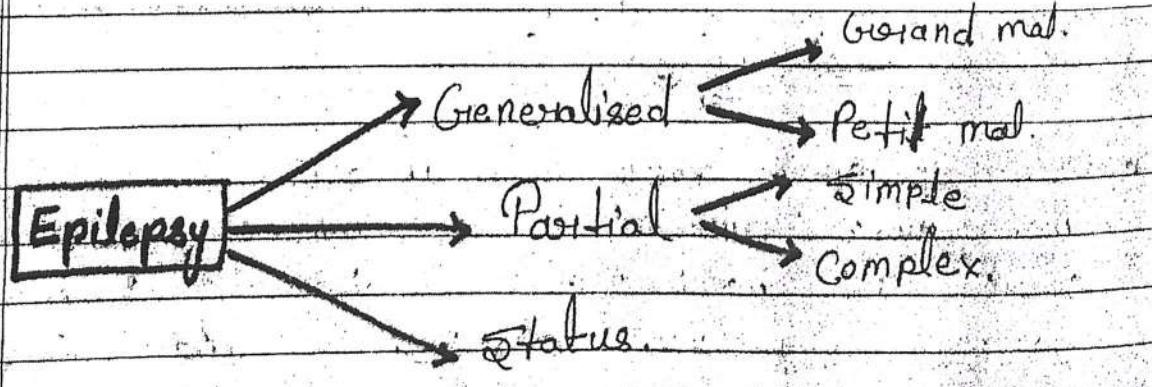
- Seizure - paraxysmal events due to abnormal excessive neuronal activity in the brain cortex.
- The clinical characteristics of seizure are result of the area of brain that is abnormally stimulated.
- 5 - 10 % of the population will have at least one seizure in their lifetime.
- Highest incidence is in childhood and late adulthood.

Symptoms -
- Chronic recurrent proximal changes
- Loss of conciousness
- Excessive of muscular activity.
- Abnormal sensation.
- duration sec - minute.

Classification of Epilesy



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[A] **Generalised** - Entire brain envolve in seizures. it is not derived arrived from any single part of the brain.

It is of 2 types -

[A] **Grandmal / Tonic clonic seizure** -

It is also called tonic clonic seizure.

In the seizure begning is start from aura. then after bilateral muscular Jurk.

In this seizure the loss of consciousness completly envalve and mubble spasm.

It remain for 2 - 5 minutes.

[B] **Petimal** - It is also called absence seizure. It is basicly appear in children.

It this seizure also the completyl loss of consciousness and loss of speen generally seen.

It last for 1 - 30 second.

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[2] **Partial / Focal** - This type of seizure is generally seen any part of brain basicaly temporal lobes.

It not envalve in full brain, and its symptoms start from (beginning) local body organ.

It is of two types -

[A] **Simple** - This is also called Jacksonion Motor epilepsy.

- It is basically certain part of brain. cortex.
- Some muscle - thumb, toe.
- Donot loss of conciousness and time duration - 1 - 2 minutes.

[B] **Complex** - It is also called Psychomotor.

- Uncommon (Patient found in rare case)
- Extensive swalling, chewing.
- Confusion, bizzare.
- Time duration - 1 to 2 minutes.

[3] **Status** - In this type of seizure, the brain damage of patient.
The time duration of seizure 30 min.

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Classification of Anticonvulsant

1. Barbiturate - Phenobarbitone
2. Deoxybarbiturate - Primidone
3. Hydantoin - Phenytoin, Fosphenytoin.
4. Iminostilbene - Carbamazepine, Oxcarbazepine
5. Succinimide - Ethosuximide
6. Aliphatic carboxylic - Valproic acid
   Sodium valproate,
   Divalproex.
7. Benzodiazepines - Clonazepam
   Diazepam
   Lorazepam
   Clobazam
8. Phenyltriazine - Lamotrigine.
9. Cyclic GABA - ~~Gd~~ Gabapentin
   Pregabalin.
10. Newer Drugs - Topiramate
    Zonisamide
    Levetiracetam
    Vigabatrin
    Tiagabine
    Lacosamide

Deoxybarbiturat

Trick → हाय बार्बर देव अली

↓ Hydantoin ↓ Barbiturate ↓ Aliphatic carboxylic acid

इनमें सक्सेस पाना है तो

↓ Iminostilbene ↓ Succinimide ↓ Phenyltriazin

बन जाओ सन्यासी इन नए चक्कर में नापड़े

↓ Benzodiazepines ↓ Newerdrugs ↓ Cyclic GABA

MODE OF ACTION

3 group →
- Facile fate GABA → Barbiturate, Deoxy. barbiturate, Benzodiazepines
- Block neuronal ion channel → Hydrantoin, Succinamide
- Unknown → Valproate.

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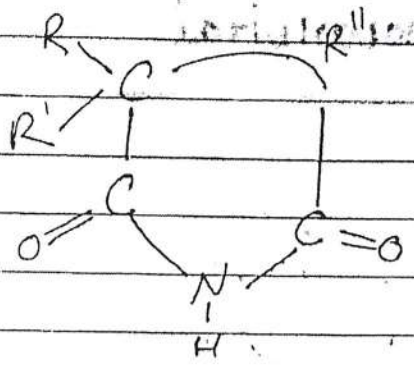
SAR of Anticonvulsants Drugs



- In the common structure of anticonvulsant drug, two carbonyl group is present, it is essential for the activity.
- 2° amine is present in the ring it is essential for the activity.
- 2 alkyl group is attached to the carbon, it is essential for the activity.
- In the carbon chain when the both R and R' is attached with the long carbon chain then their activity is for generalised seizure is Yes and for absence seizure is Yes.
- In this ring when we add any aromatic rin the activity for generalised seizure is Yes and for absence seizure is Yes.

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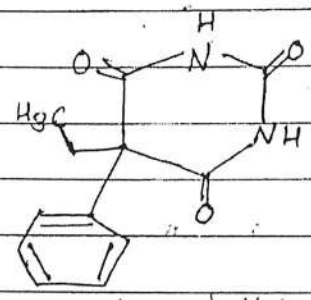
Brief Notes on Drugs of Antiepileptic or Anticonvulsant

1. Phenobarbital



- Phenobarbital is chemically 5 - ethyl - 5 - phenyl - 1 - 3 - diazine - 2,4,5 - trione.
- It is the drug of choice and is used virtually in all the three types of epileptic seizure viz. grand mal, petit mal and psychomotor.
- It binds to an allosteric site on the $GABA_A$ receptor and it enhances the GABA receptor mediated current by prolonging the opening of the chloride channels. It leads to membrane hyperpolarization and ultimately synaptic inhibition and hence neuronal excitability.
- It also blocks excitatory responses induced by glutamate.

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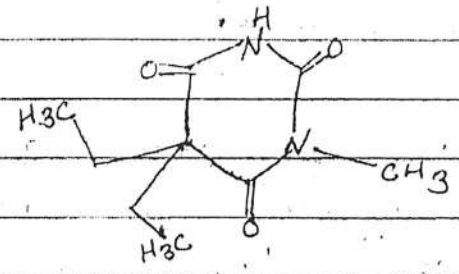
- It has a long half-life time and therefore it will take a few weeks before reaching a therapeutic and effective level
- The main side-effects of Phenobarbitone are drowsiness, especially during the 1st week of treatment.

Uses - • Phenobarbital is a barbiturates that is widely used as a sedative and anti-seizure medication.

- It is used in idiopathic generalized epilepsies
- It is also reasonably effective in other generalized seizures and in partial seizures.

2. Methabarbital



- Methabarbital is chemically, 5,5-dimethyl-1-methyl-1,3-diazinane-2,4,6-trione
- It is mostly demethylated to barbital in vivo. Also it possesses more sedating property than phenobarbital.

- It could be safely recommended for grand mal seizures.

It binds at a distinct binding site associated with a chloropore at the GABA receptor, Tesing the duration of time for which the chloropore is open.

Uses - Methabarbital has similar properties to phenobarbital and is used in the treatment of epilepsy.

- It is also used for the treatment of short term insomia.
- It belongs to CNS depressants group that induce drowsiness and relieve tension or nervousness.

3. Hydratoins

Hydratoins are close structural relatives with barbiturate, only differing in lacking the 6-oxo group. They passes imidazaline-2-4 diane heterocyclic ring system.

Hydantoins used in treatment of generalized tonic-clonic seizure.

- When two alkyl substituents groups are replace with R_1 and R_2 at carban no. 5 then activity will enhance multiple no. of times.

- When the C chain length is ↑es in both alkyl position then their lipophilic nature is ↑es and they can cross the BBB and their potency and duration of action is ↑es.

- At the alkyl substitution when the C chain length upto 5 to 6 carban (pentyl to hexyl C) then activity will ↑es but when the C chain increase up after 6 from 7 to 9 (heptyl to nonyl) then their activity ↓es due to ↑es their molecular size.

- When in the alkyl substituention the branching of C chain is ↑es and cyclic group is attached with the branch then their activity will be ↑es.

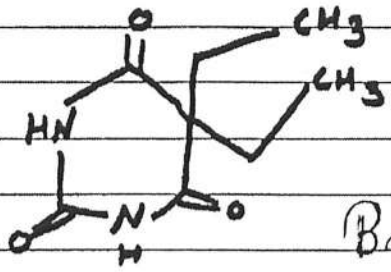
- When both alkyl group is replaced with the phenyl group ring then their lipophilicity is ↑es and their structure activity is ↑es.

- At the position no. 1 and 3 any one hydrogen atom is replace with alkyl group then their activity ↑es.

- At position 1 and 3 when both hydrogen is replaced with alkyl group then their activity ↓es and it become pharmacokinetically unstable because their water solubility completely lessed.

Brief Notes on Barbiturate Drugs

[1] Barbital

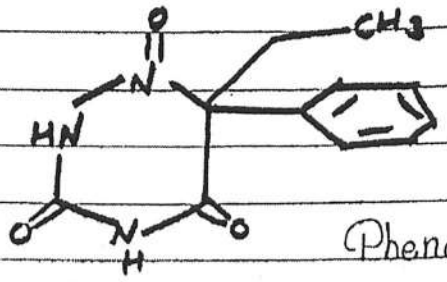


Barbital.

- Barbital is chemically 5,5-dimethyl-2,4,6 (1H, 3H, 5H)-pyrimidinetrione.
- It is also known as barbitone which is chemically 5,5-diethyl barbituric acid, the first commercially available barbiturate.
- It tones the activity of the inhibitory neurotransmitter GABA to the $GABA_A$ receptor which results in inhibitory effect on the CNS.

Uses- Barbital is used as a hypnotic and antiepileptic.

[21] Phenobarbital



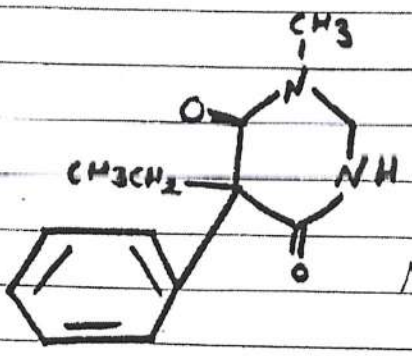
Phenobarbital

- Phenobarbital is chemically, 5- ethyl - 5- phenyl - barbituric acid
- It is a long acting barbiturate derivative and also known as phenobarbitone, which is the oldest, but still used as anti-epileptic medication.
- It tases the activity of the inhibitory neurotransmitter GABA to the $GABA_A$ receptor which results in tased influx of chloride ions leading to tased excitability.
- It is also produces blockade of excitary glutamate signaling.
- Phenobarbital is a CYP450 inducer and hence dosing of other drugs is needed to be monitored.

Uses-

- Phenobarbital is used a sedative, hypnotic and also as an anticonvulsant for both generalized tonic-clonic and partial seizures.
- It is occasionally used to treat drug withdrawal as a pre anaesthetic medication, Crigle-Najjar syndrome and Gilbert syndrome patients to aid in the conjugation of bilirubin

[31] Mephobarbital



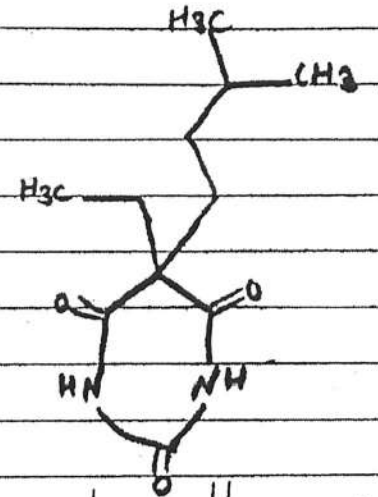
Mephobarbital.

- Mephobarbital is chemically 3-methyl-5-ethyl-5-phenylbarbituric acid.
- It is a long acting barbiturate derivative, as the parent drug, it undergoes metabolically N-demethylated phenobarbital and responsible for its activity.
- It increase the activity of the inhibitory neurotransmitter GABA to the $GABA_A$ receptor which results in inhibitory effects on CNS.

Uses- • Mephobarbital is used as a hypnotic and as an anticonvulsant.

Intermediate Acting Barbiturates
(Duration of action = 3-6 hours)

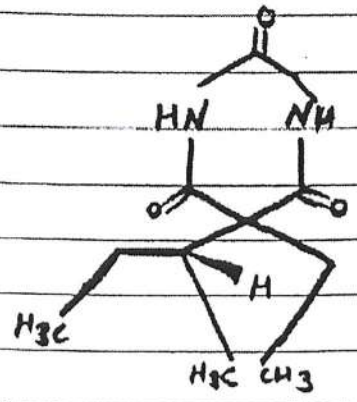
[1] Amobarbital



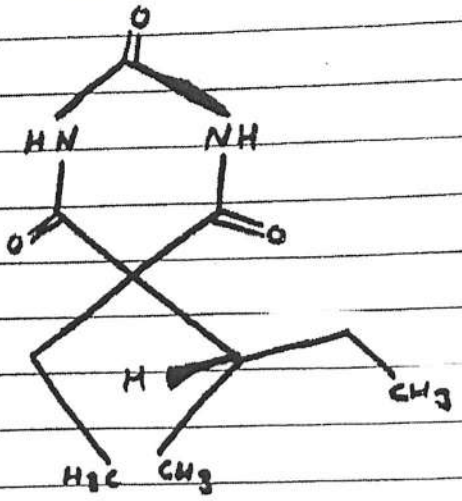
- Amobarbital is chemically, 5-ethyl (3-methylbutyl)-2,4,6-(1H, 3H, 5H)-pyrimidinetrione.
- It is also known as amylobarbitone, which an intermediate acting barbiturate with moderate duration of action 4-5 hours.
- It Teses the activity of the inhibitory neurotransmitter GABA to the $GABA_A$ receptor which results in Tesed influx of chloride ions leading to tesed excitability.

Uses- • Amobarbital is used as sedative and hypnotic.

[27] Butabarbital



(S) - Stereoisomer



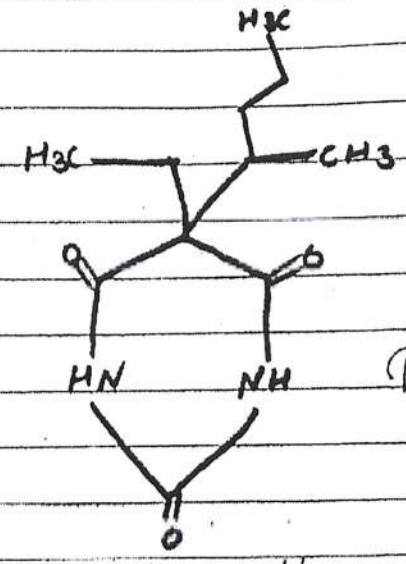
(R) - Stereoisomer.

- Butabarbital is chemically, 5-ethyl-5-(1-methylpropyl)-2,4,6(1H,3H,5H)-pyrimidinetrione.
- It is an intermediate acting barbiturate with moderate duration of action of 3-6 hours.
- It tases the activity of the inhibitory neurotransmitte GABA to the GABA$_A$ receptor which results in tased influx of chloride ions leading to tased excitability.
- It has a particularly fast onset of effects and short duration of action. has importance in management of severe and relieving anxiety before surgical procedure.

Uses - • Butabarbital is used as sedative and hypnotics.

Short acting barbiturates (Duration of action < 3 hours)

[1] Pentobarbital



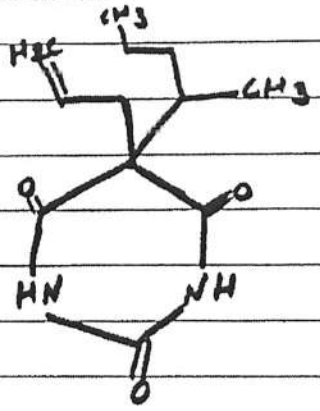
Phenobarbital

- Pentobarbital is chemically, 5-ethyl-5(1-methylbutyl)-2,4,6(1H, 3H, 5H)-pyrimidinetrione.
- It is a short acting barbiturate with duration of action less than 3 hrs.
- It raises the activity of inhibitory neurotransmitter GABA to the GABA$_A$ receptor which results influx of chloride ions leading to raised excitability.

Uses-
- Pentobarbital is used as sedative and hynotic.

- It also finds importance as a preanesthetic medication and in control of convulsions in emergencies.
- It has an application in reducing intracranial pressure in Reye's syndrome, traumatic brain injury and induction of coma in cerebral ischemia patients.
- It is also used as veterinary anesthetic agent.

[2] Secobarbital



Secobarbital.

- Secobarbital is chemically 5-(1-methylbutyl)-5(2-propenyl)-2,4,6(1H, 3H, 5H)-pyrimidinetrione.
- It is short acting barbiturate derivative.
- It Teses the activity of the inhibitory neurotransmitter GABA to the GABAA receptor which results in Tesed influx of chloride ions leading to Tesed excitabili

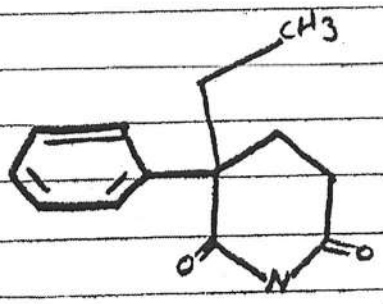
Uses - • Secobarbital is used as an anaesthetic, anticonvulsant, anxiolytic, sedative and hypnotic drug.

Miscellaneous Sedative and Hypnotic Derivates

A wide range of chemical structure (eg imides, amides, alcohols) can produce sedation and hypnosis resemblimbling those produced by the barbiturates.

[I] Amide and Imide Derivative

1. Glutethimide



Glutethimide

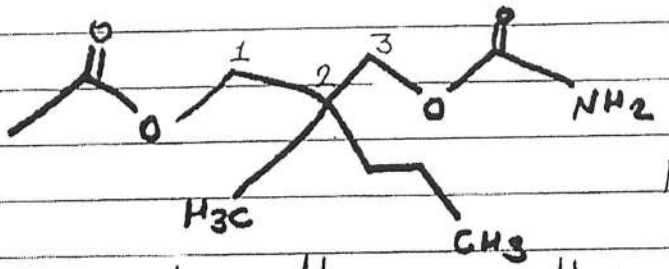
- Glutethimide is chemically, 2- ethyl-2- phenyl glutarimide.
- It is one of the most active non-barbiturate hypnotics that is structurally similar to the barbiturates.

- Glutethimide is highly lipophilic and undergoes extensive oxidation metabolism with half-life period of approximately 10 hours.

Uses - • It is used as sedative and hypnotics.

(II) Alcohols and their Carbamate Derivatives

1. Meprobamate



Meprobamate.

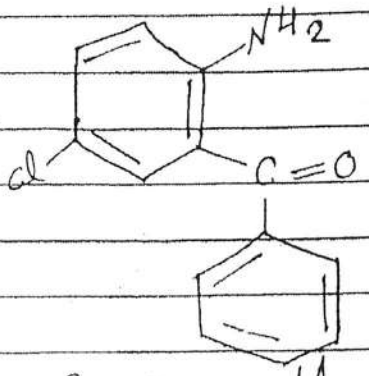
- Meprobamate is chemically 2-methyl-2-propyl 1,3 propanediol dicarbamate.
- Meprobamate doesnot act through GABA system.
- It has inter-neuronal blocking properties at level of the spinal cord, and responsible for its skeletal muscle relaxation.

Uses - • Meprobamate is indicated as an antianxiety agent also an a sedative and hypnotic agent.

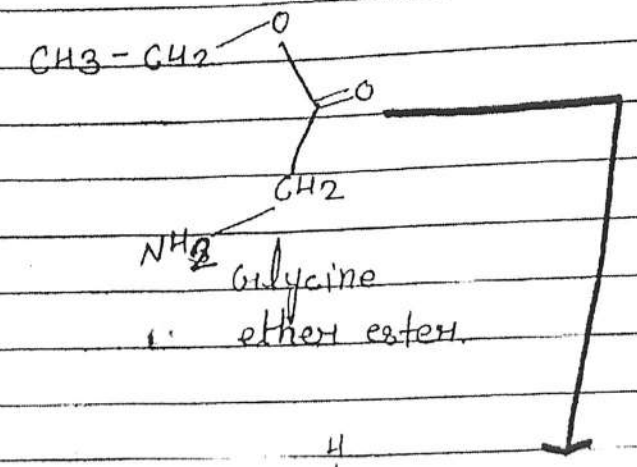
- It is also effective against absence seizures and also a centrally acting skeletal muscle relaxant.

Synthesis of Diazepam and Barbital

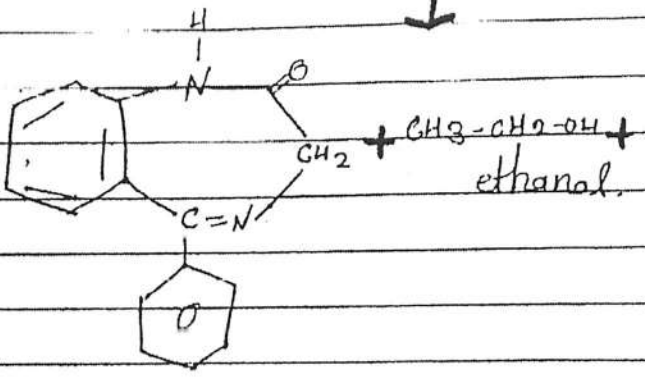
1. Diazepam -



2 amino 5 chloro Benzophenone



Glycine ethyl ester.

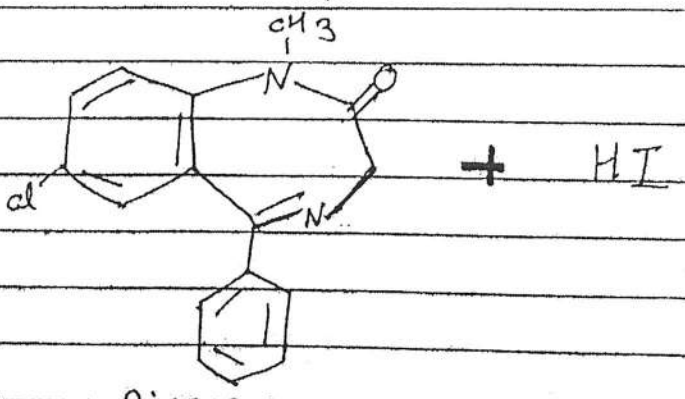


ethanol.

$AlCl_3$

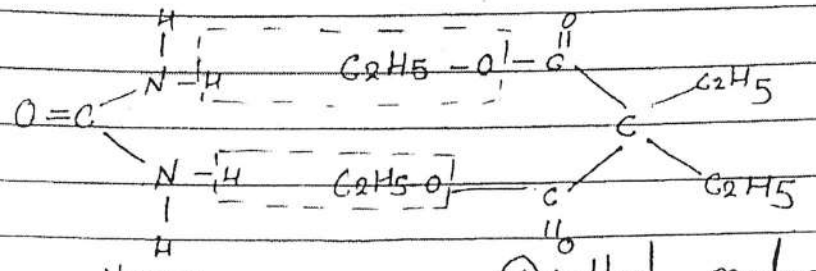
Methylation

CH_3-I



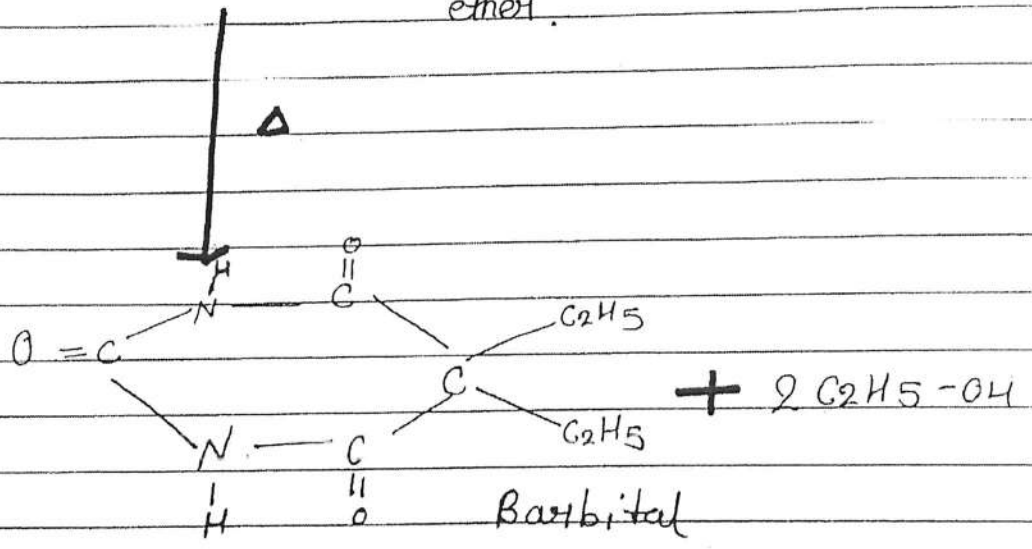
Diazepam.

2. Barbital



Urea

Diethyl malonic ether



Barbital

Date
27/4/2020

Day - Monday

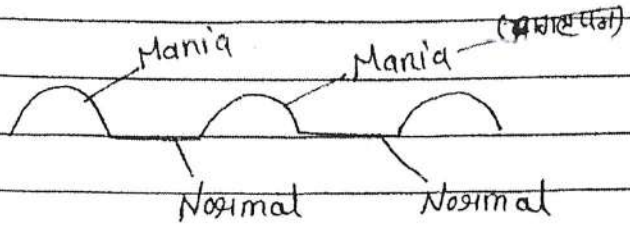
Chapter - 2

ANTIPSYCHOTICS

- Psychosis is a type of Mental Health issue.
- Psychosis is a disease is a mental health disorder, in which the patient loose contact with the social, they shows the abnormal behaviour their thiking capacity their activity their gesture, their posture, their speech therapy all things are disturbs this is called psychosis.
- When the patient generally normal but in certain case in any time they shows the psychochit symptoms this is called one of episode.
- Sychosis is devided into 2 class -
  A. Schizophrenia
  B. Bipolor disorder.

[A] Schizophrenia - In this situation the patients are fully mently disturb. they are in exicted stage they perform all these function against the society and they have no control their activities, voice anything.

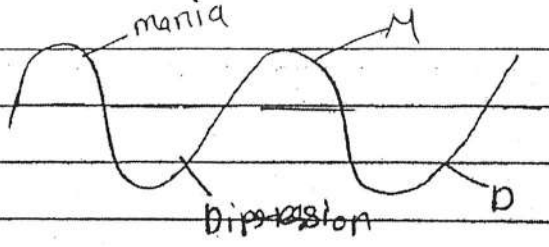
Schizophrenia is a unipolar disorder



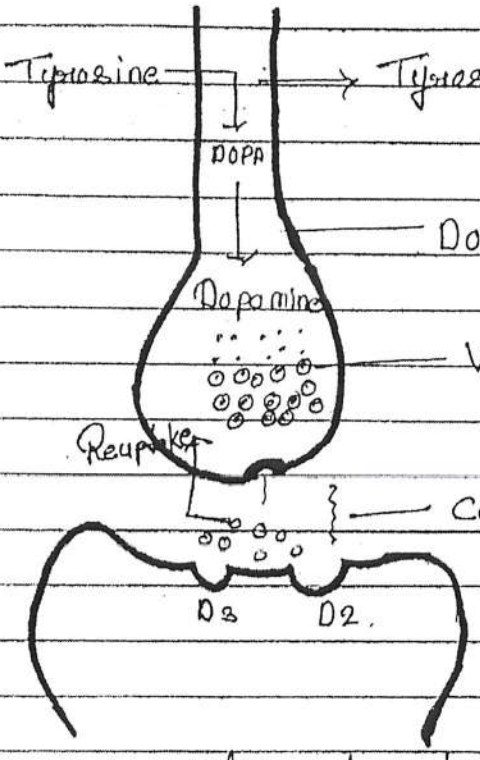
Bipolar disorder- Bipolar disorder depends upon two situation Mania situatio and dipression situation

Mania situation is same as schizophrenia disorder. persons shows extra activity. and exaitment. but in the case of depressio the persons becomes extra silent. upset show suicide symptoms. no talk to anyone. not eat etc.

The shows episodes b/w mania and dipression they shows up and down situation is called bipolar disorder.



- Dopamine is a neurotransmitter which is catacholamine in nature, which is responsible for the activity of brain.
- It is synthesize in the neurons by the help of Tyrosine -



- When the vessicles of dopamine is release into synaptic cleft then they bind with the D2 and D3 receptor and the brain becomes extra activated / Excited.
- In the synaptic cleft there are reuptake of dopamine and there is a enzyme COMT (catichol -o- methyl transferase) which degrade the Dopamine, but the COMT enzyme is

inhibited and reuptake is also inhibited then the level of dopamine is release multiple times and in it causes the psychosis.

Characteristics of Psychosis

- Loss of connectedness with reality.
- Feeling of very anxious or agitated
- Have very low or high moods.
- Persons may develops false ideas or beliefs about reality.
- Persons may have false perceptions.
- Persons also experience flaws in the ways they think (thought disorders)
- Persons may think that people are against them and they may hear voices or sounds that are not real.
- Poor physical health.
- Significantly impairs work, family and social functioning.

Classification of Antipsychotic Drugs (Neuroleptics)

1. Phenothiazines ⟶ फेंकते हैं सबकुछ
2. Butyrophenones ⟶ बतियाते हैं खुद से
3. Thioxanthenes ⟶ ठोकर खाते हैं
4. Other heterocyclic's ⟶ औरों के साथ
5. Atypical antipsychotics ⟶ असामान्य से रहते हैं।

1. Phenothiazines -

Aliphatic side chain - Chlorpromazine
Triflupromazine

Piperidine side chain - Thioridazine

Piperazine side chain - Trifluoperazine
Fluphenazine

Trick: ~~फेंकते हैं सबकुछ~~ पिन्न की वाह
CFT3.

2. Butyrophenones -

Haloperidol
Trifluperidol
Penfluridol

Trick - बतियाते हैं खुद Doll से -
हैलो प्रिया तेरे फ्लैट में न फ्लू है।

3. Thioxanthenes - Flupenthixol

Trick - थोकरे खाते हैं फूलों पे नहीं।

4. Other heterocyclic's - Pimozide, Loxapine.

Trick - औरों के साथ पी लो ज्यादा पानी

5. Atypical antipsychotics -

Quetiapine
Olanzapine
Aripiprazole
Clozapine
Amisulpiride
Zotepine
Risperidone.

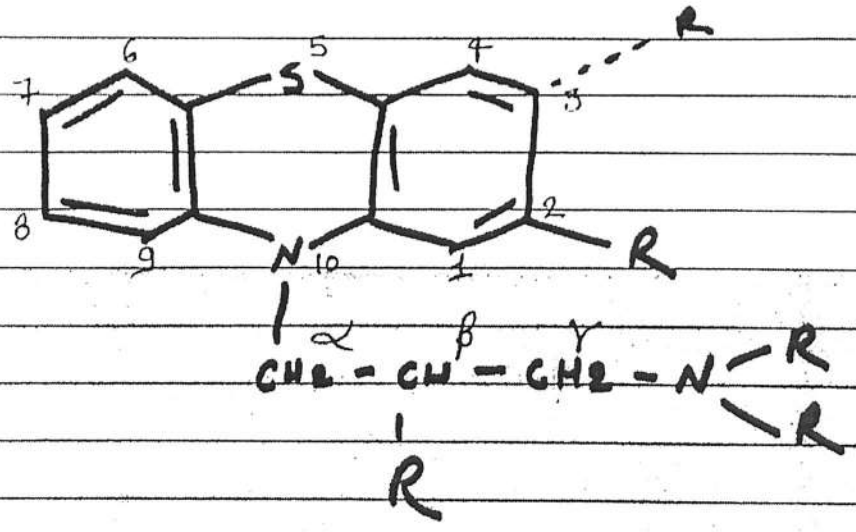
Trick - असामान्य

कुतिया आलू और काला जाप अमरीश पुरी के जूते पे रस गिरा दो

SAR of Phenothiazine

- For the antipsychotic activity of drug 3 fused ring is essential for the activity.
- Sulfur at position 5 and Nitrogen at position 10 is essential for activity.
- A position no. 10 Nitrogen atom aliphatic chain is essential for the activity.
- At the position no. 2 if we add any e^- withdrawing group like Cl, F, Br, I then they ↑es the activity multiple no. of times.
- At the position no. 2 if we add any e^- donating group / e^- releasing group / +I group then the activity of antipsychotic phenothiazine is ↓es.
- At position no. 3 when we add any e^- withdrawing group then their activity is ↑es but as compare to substitution at point 2 there activity not as much ↑es.
- At position no. 1 and 4 if we use any substitution group then their activity is ↓es.

- The distance b/w aliphatic N and ring N it should be minimum 3 Carbon if we ↑es the C chain or ↓es the C chain then their activity is ↓es.
- In N and β carbon when we use the long chain hydro carbon at the position of R then their lipophilicity ↑es and their activity for crossing BBB is ↑es and their duration of action also ↑es on body.
- At the position α and γ in aliphatic amine chain when we use any substitution their activity will ~~↑es~~. ↓es.



Brief Notes on Phenothiazine Drugs

[1] Promazine Hydrochloride

- Promazine HCl is chemically, N, N - dimethyl - 3 - phenothiazin - 10 - yl - propan - 1 - amine hydrochloride.
- Promazine HCl blocks postsynaptic dopamine receptor D_1 and D_2 mesolimbic receptors and thus stimulation of psychotic effects, such as hallucinations and delusions.
- It also blocks medullary chemoreceptor trigger zone (CTZ), of vomiting center and thus acts as antiemetic.
- It also blocks alpha - adrenergic receptors and exhibits strong anticholinergic activity.

Uses -

- It is primarily used as antipsychotic agent in short - term treatment of disturbed behaviour.
- It is also used as antiemetic.

[2] Chlorpromazine Hydrochloride

- Chlorpromazine hydrochloride is chemically, N-dimethyl-3 (2-chlorophenothiazine) - 10-yl) propan-1-amine, hydrochloride.
- It exerts as its antipsychotic effect by blocking postsynaptic dopamine receptors in cortical and limbic areas of brain and thus preventing the excess of dopamine in the brain. ~~and thus preventing~~
  Thereby it leses stimulation of psychotic effects such as hallucinations and delusions.
- It also blocks dopamine receptors in the chemical trigger zone (CTZ) in the brain, thereby relieving nausea and vomiting.

Uses- • Chlorpromazine hydrochloride acts as an antipsychotic agent used to treat hallucination and delusion.

[3] Trifluperazine Hydrochloride

- Trifluoperazine hydrochloride is chemically, 10(3-(4-methylpiperazin-1-yl) propyl] -2-(trifluoromethyl) phenothiazine, hydrochloride.

- It blocks central dopamine receptors and is used to treat delusions and hallucinations caused by an excess of dopamine.
- It also blocks the postsynaptic dopamine D_2-receptor in the chemoreceptor trigger zone (CTZ) of the brain and may b prevent emesis.
- It also blocks central adrenergic receptors and leads to anxialytic effects.

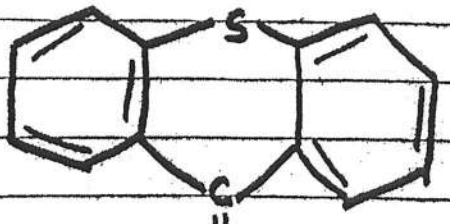
Uses -
- Trifluoperazine is piperazine phenothiazine derivative and antipsychotic agent. that is no longer commonly used in clinical practice.
- It also possesses anxialytic, and antiemetic activities.

Ring Analogue of Phenothiazines

[A] Thioxanthene Derivative

Most

1. Chlorprothixene



Chlorprothixene.

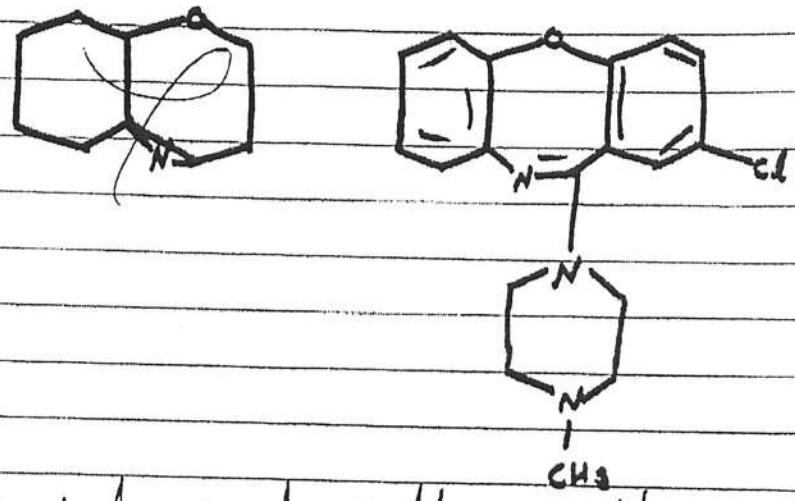
- Chlorprothixene is chemically, 3-(2-chlorothioxanthen-9-ylidene)-N, N-dimethyl-propan-1 amine.
- It is a tertiary amine typical antipsychotic drug of thioxanthenes class.
- It produces its antipsychotic action by blocking the 5-HT2 D1, D2 and D3 receptors.
- It also possesses histamine (H_1) muscarinic and α-1 adrenergic receptors blocking action.

Uses:-
- Chlorprothixene is used as 1st generation antipsychotic.

It also has non-narcotic analgesic, antiemetic, sedative and cholinergic antagonist activity.

Imp [B] Dibenzoxazepine Derivative

1. Loxapine Succinate



- Loxapine succinate is chemically 8-chloro-6-(4-methyl piperazin-1-yl) benzo[b][1,4] benzoxazepine, butanedioic acid.
- It produces its action by blocking the dopamine receptors at postsynaptic receptor sites in the limbic system, cortical system and basal ganglia, there by reducing the hallucinations and delusions.

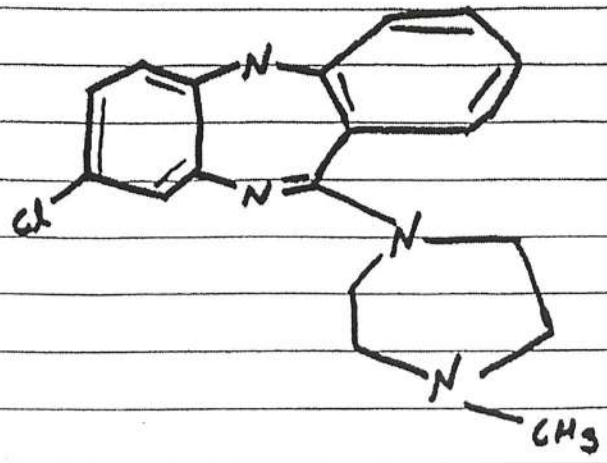
Uses- • Loxapine succinate is an antipsychotic agent used in schizophrenia.

It also possesses antiemetic, sedative, anticholinergic and antiadrenergic actions.

V.V most

[C] Dibenzodiazepine Derivatives

[1] Clozapine



clozapine.

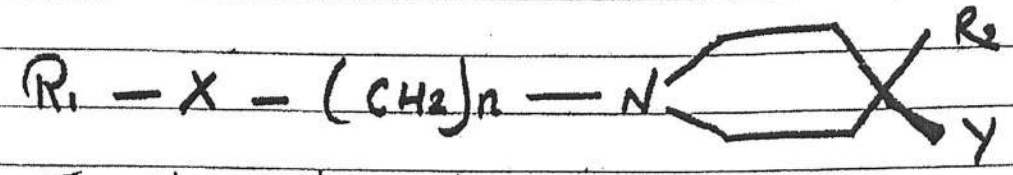
- Clozapine is chemically 3-chloro-6-(4-methylpiperazine-1-yl)-5H benzo [b] [1,4] benzo-diazepine.
- It is an important atypical antipsychotic.
- It weakly blocks D_2 receptors and relieves schizophrenic symptoms such as hallucinations, delusions and dementia.

Uses- • Clozapine is an important atypipsychotic.

It use is restricted because of a relatively high frequency of agranulocytosis as a severe side effect.

SAR of Flurobutyrophenones

Structure -



[1] In the Flurobutyrophenones structure the aliphatic nitrogen is attached with the ring which is essential for the activity.

[2] Attach the Nitrogen with aliphatic chain of C. which is essential for the activity.

[3] At R_1 position if we use any aromatic ring containing F atom at para position then it had the maximum antipsychotic activity.

[4] In Flurobutyrophenoes ring at the position of X when we use carbonyl group or ketone group then they have the maximum antipsychotic activity, but in the case of when use aldehyde (CHO) and alcohal (CH-OH) then also their activity ↑es.

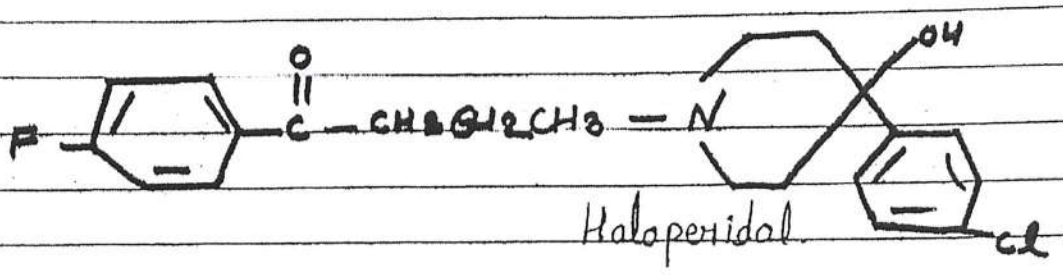
[5] In the aliphatic chain when n = 3 (it means propyl) then activity is maximum, when we ↑es or ↓es the no. of Carban chain then antipsychotic activity of Flurobutyrophenes is ↓es.

[c] In the Fluorobutyrophenoes ring at the position no. R_2, when we use aliphatic chain or aromatic ring then their activity is ↑es but ↓ when we use aromatic ring then their activity is maximum.

[d] In Fluorobutyrophenoes ring at the position of Y when we use ↓ alcohal and chlorine then their activity is ↑es but when we use alcohal then their activity is maximum.

Brief Notes on Fluorobutyrophenone Category Drugs

1. Haloperidal

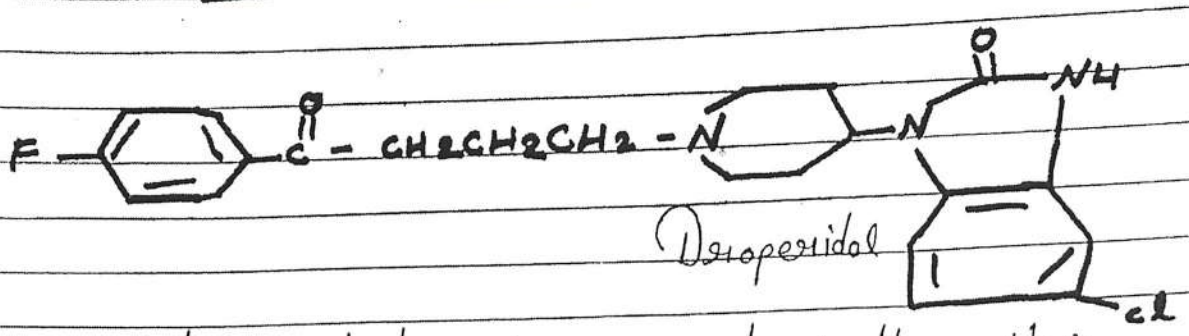


Haloperidal

- Haloperidol is butyrophenone chemically it is 4-[4-(4-Chlorophenyl)-4-hydroxy-piperidin-1-yl]-1-(4-fluorophenyl) butan-1-one.
- It competitively blocks postsynaptic dopamine receptor in the mesolimbic system of brain and so is used to treat delusion and hallucination.
- It has strong affinity for D_2 and D_3 receptors.
- It blocks dopamine receptors in the chemoreceptive trigger zone (CTZ) and leads to its anti-emetic effects.

Uses-
- Haloperidal is a typical antipsychotic drug.
- It is a potent antipsychotic useful in schizophrenia and in psychoses associated with brain damage.
- It also possesses neuroleptic and antiemetic activities.

2. Droperidol



Droperidol

- Droperidol is butyrophenone, chemically it is 3-[1-(4-(4-fluorophenyl)-4-oxybutyl]-3,6 dihydro-2H-pyridine-4-yl]-1H-benzimidazol-2-one.
- It has general properties similar to those of haloperidol.
- It acts by blocking dopamine D2 receptors.
- It blocks dopamine receptors in chemoreceptor trigger zone (CTZ) and leads to antiemetic effect
- It also acts on postsynaptic GABA receptors in the CNS and reses the inhibitory effect of GABA which leads to sedative and anti-anxiety activities.

Uses - • Droperidal is used as preanesthetic neuroleptic
- It is used in combination with an opioid analgesic agent fentanyl preanesthetically.
- It also possesses anti-emetic, sedative and anti-anxiety properties.

Unit - V

Date: _____ Page: _____

General anaesthetics

* These are the drugs which induce the excess of perception of all sensation and loss of pain.

* These are the drug which act like CNS depressant.

* There are basically four stages of anaesthesia —

Stages of anaesthesia

Stage-1 → Analgesia

Stage-2 → Delirium

Stage-3 → Surgical anaesthesia

Stage-4 → Medullary paralysis

Stage-1 → Analgesia →

This stage starts with the first intake of the anaesthetic and ends with the onset of consciousness.
↓ loss of

Date: Page:

Stage-2 :- Delirium :-

This stage begins with loss of consciousness : patients feels like hallucination, emotions almost finished or over, patients may shout and the eyes may be dilated.

Stage-3 :- Surgical anaesthesia :-

This stage is the actual stage of unconsciousness.

In this stage respiration is full and regular with small pulses, and pupils become constricted.

All the surgical procedures are carried out in this stage.

Stage-4 :- Medullary paralysis :-

This stage begins with the central respiratory paralysis and ends with cardiac failure and death.

This stage should be avoided.

Date: _____ Page: _____

Classification

- General anaesthetics
  - Inhalational Anaesthetics
    - Gas
      - N_2O (nitrous oxide)
    - Volatile
      - Ether
      - Halothane
      - Isoflurane
      - Desflurane
      - Sevoflurane
      - Methoxyflurane
      - Enflurane
  - Intravenous Anaesthetics
    - Fast acting
      - Thiopental
      - Methohexital
      - Propofol
      - Etomidate
    - Slow acting
      - Diazepam
      - Lorazepam
      - Midazepam

Date: _____ Page: _____

General anaesthetics classification

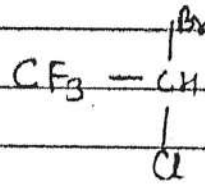
General anaesthetic

- Inhalation
  - Gas
    - Nitrous oxide
  - Volatile
    - Ether
    - Halothane
    - Isoflurane
    - Desflurane
    - Sevoflurane
    - Methoxyflurane
    - Enflurane
- Intravenous
  - Barbiturates
    - Methohexital
    - Thiamylal
    - Thiopental
  - Dissociative
    - ketamine
  - Opioids
    - Morphine
    - Fentanyl
    - Sufentanil
    - Alfentanil
  - Benzodiazepines
    - Diazepam
    - Midazolam
  - other
    - Etomidate
    - Propofol

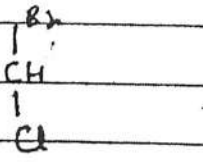
Date: _____ Page: _____

Halothane

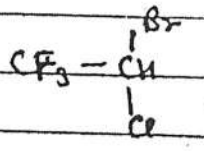
structure →



Syn →

(i) $CF_3-CH_2-Cl \xrightarrow[\Delta\ 465°C]{Br_2}$ 

1 chloro 2,2,2 trifluoro ethane

(ii) $CF_3-CH_2-Br \xrightarrow[\Delta\ 380°C]{Cl_2}$ 

1-Brom . 2-trichloro ethane

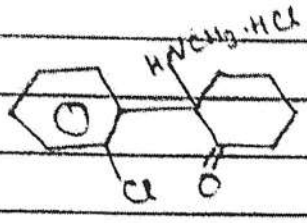
Uses

* Used as general anaesthetic.
* It's beneficial point an advantages is that is does not ↑ the products of saliva-

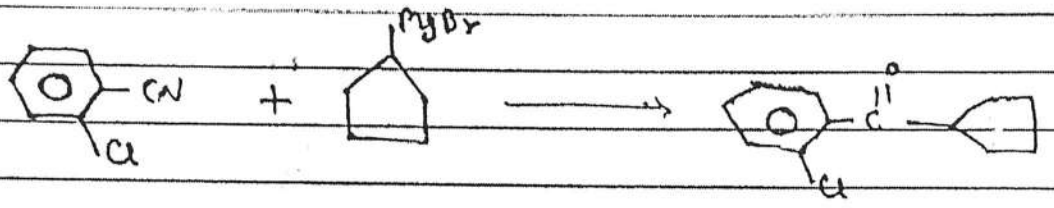
Date: _____ Page: _____

Ketamine : HCl

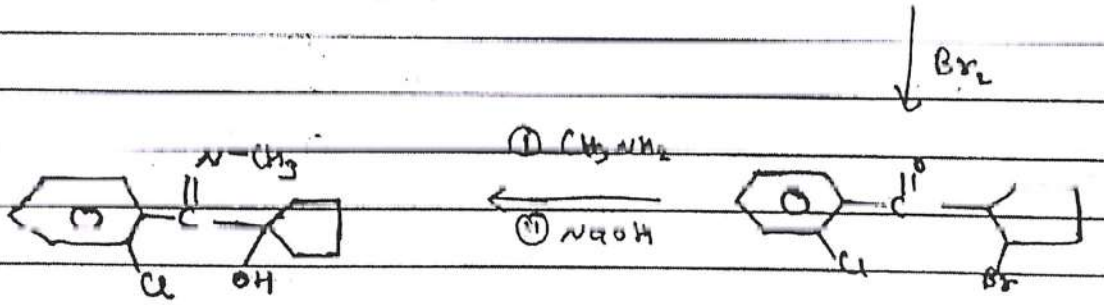
str-:



Syn -:



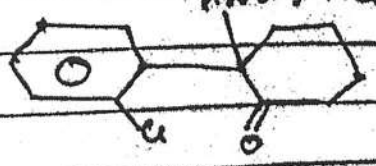
o-chloro benzonitrile



① Δ HCl

② Ring expansion

③ Tautomerism



Date: _____ Page: _____

Uses

* It induces the sedation so it helps in pain relief.
* Used as general anaesthetic.

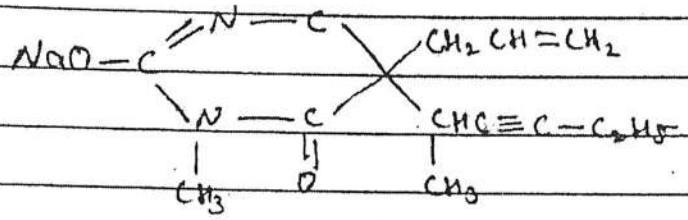
Side effect :-

It produce some memory loss and depression.

Date: _____ Page: _____

Methohexital sodium

Str →

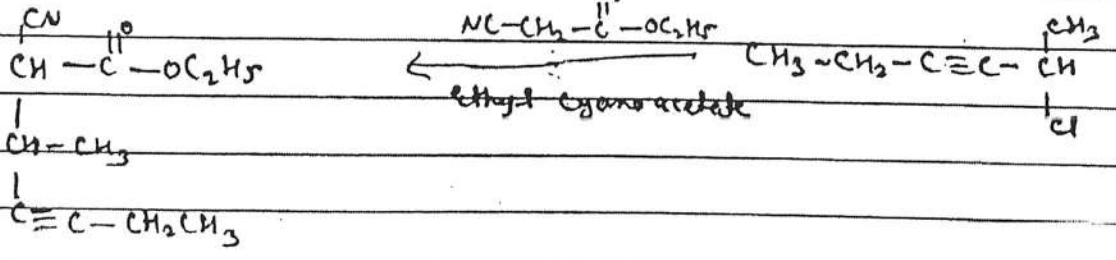


Syn →

$CH_3CH_2C\equiv C-MgBr$ —(CH_3CHO, Hydrolysis)→ $CH_3-CH_2C\equiv C-\underset{OH}{\underset{|}{CH}}-CH_3$

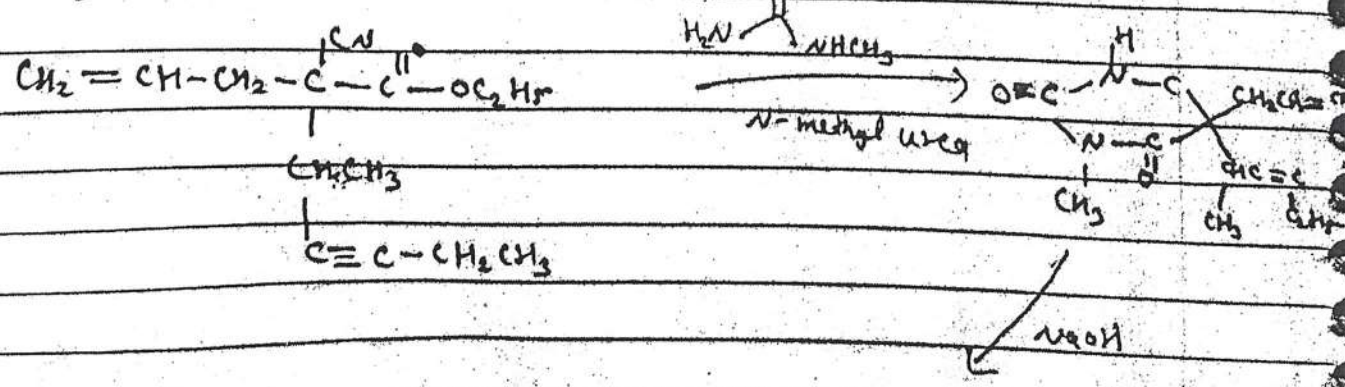
1-butyne magnesium bromide

$\downarrow PCl_5$

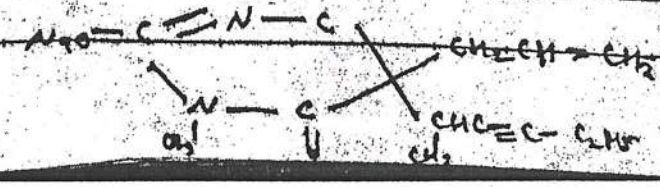


$\downarrow$ ① $CH_2=CHCH_2Br$

② C_2H_5ONa



$\downarrow NaOH$



Date: _____ Page: _____

Uses

* It is used as general anaesthetic.
* It is very important drug available and used in hospitals.
* It is commonly used to induce sedation or general anaesthesia for surgery and dental procedure.

Date: _____ Page: _____

Narcotic and non-narcotic agents

Morphine and related drugs / Analgesics :-

* The term analgesia comes from a greek word meaning without pain.

* Analgesia is the relief of pain without loss of consciousness.

* Opium has been known to relief pain since and ancient time.

* Opium is obtained from the poppy plant (papaver somniferum).

* Morphine and morphine like drugs are referred as opioids or opiates.

* The opioids defer from non-opioids analgesics in the following aspects / characteristics of opioids —

1→ Physical dependence (Addict^{n}) and tolerance is developed.

2→ They have potential for abuse.

3→ They act mainly within the CNS while non-opioids are peripheral.

4→ These are most powerful analgesics and dont

Date: _____ Page _____

reduce Inflammation.

S→ Opioid have high first pass metabolism. so they are given parenterally.

Classification

1- Morphine analogues = Morphine, Diamorphine
Codeine, Nalorphine
Levorphan, Naloxone.

2- Synthetic derivatives =

(I) Phenyl piperidine = Pethidine, Fentanyl.

(II) Methadone = Methadone and Dextropropoxyphene

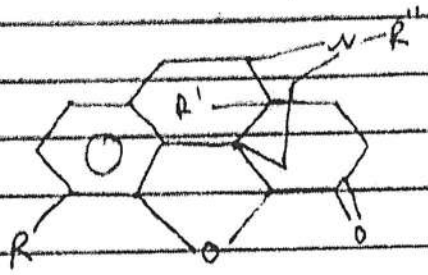
(III) Benzomorphan = Pentazocine and Cyclazocine

(IV) Semisynthetic = Etorphine and buprenorphine

Date: _____ Page: _____

SAR of morphine analoges

General structure —



SAR of morphine analoges can be summerised under following steps —

1- In the place of R hydroxy grp is important for activity. If we mask this grp by etherification, the activity is reduced to 1/10 (one by ten) of the morphine.

2- Esterification of this OH– gives compound more active than morphine.

3- If we convert carbonyl grp to hydroxy grp, the activity will reduce.

4- Replacement of N–CH_3 by N–C_3H_5 in the place of R'' resulted in slightly fall in analgesic activity.

5- In the place of R' if we substitute the hydroxy grp, the analgesic activity

Date: _____ Page: _____

is ↑.

6 - Hydrogenation of first ring produces compound with equal or superior analgesic action.

7 - Substitution other than R, R' and R'' resulted in reduction of analgesic activity.

8 - Opening of the ether bridge, breaking of ether bridge or opening of piperidine ring results in ↓ in activity

Narcotic antagonist

(a) Pure antagonist → Naloxone

(b) Partial antagonist → Nalorphine, Levallorphan

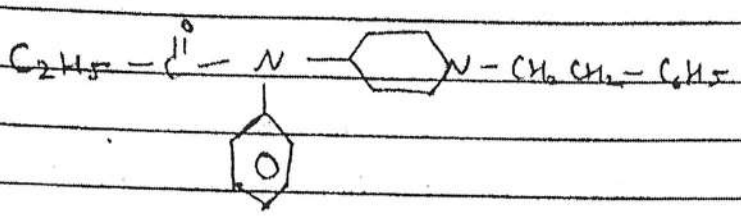
(c) Partial agonist of morphine → Propiram

LAH → $LiAlH_4$

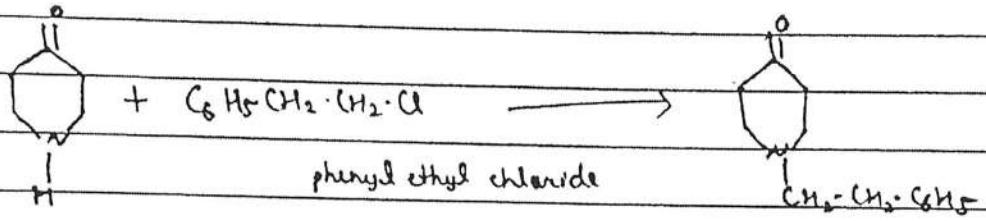
Date: _____ Page: _____

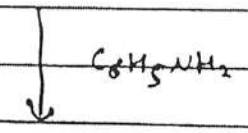
Fentanyl citrate

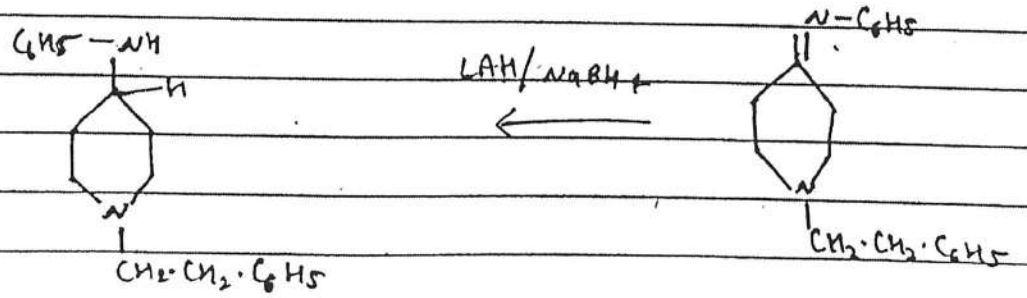
Str →

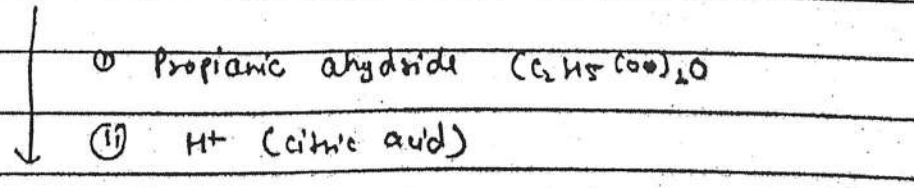


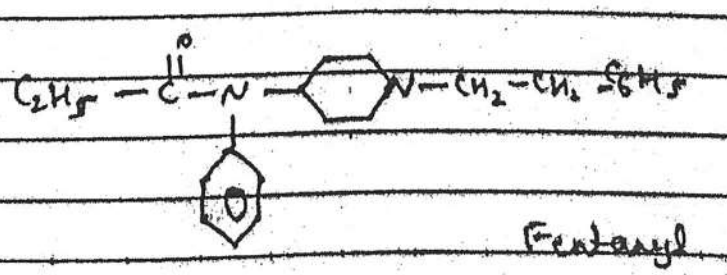
Syn →









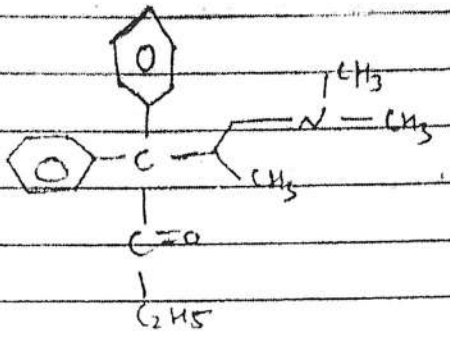


Fentanyl citrate

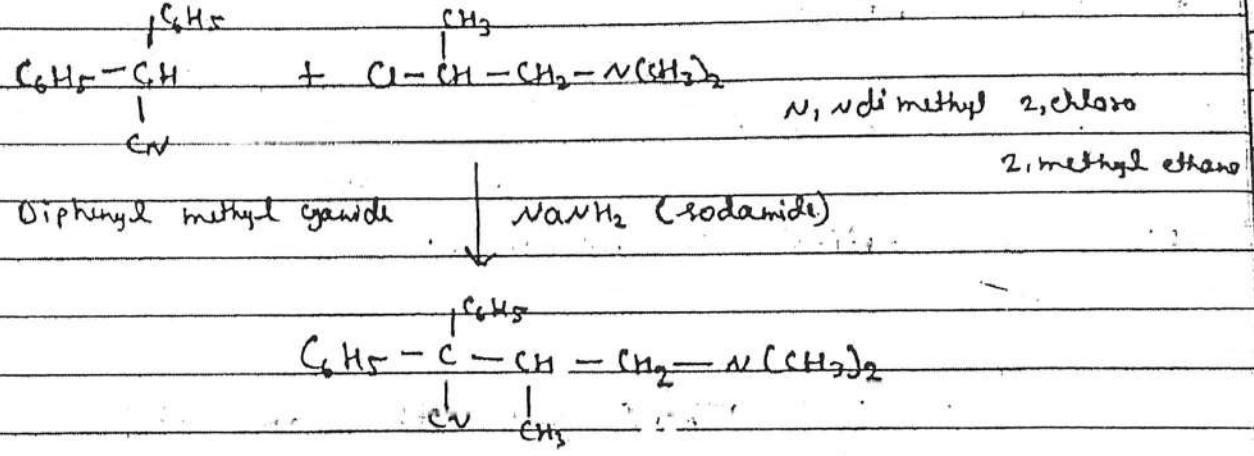
Date. _____ Page: _____

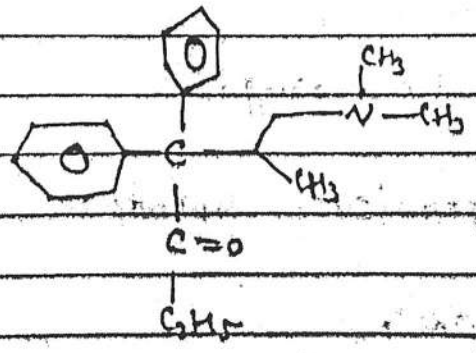
Methadone hydrochloride

Structure :-



Synthesis :-





·HCl

Metadone · HCl

Date: _____ Page: _____

NSAIDs

It stands for non-steroidal anti-inflammatory drugs.

All drugs of this categories have 3 main following action —

1- Analgesic :-
There are the agent which are used to relief pain.

2- Anti inflammatory :-
These are the agent which are used to relief inflammation.

3- Anti pyretic :-
These are the agent which are used to reduce the body temperature upto normal (98.4°F)

Characteristics of NSAIDs :-

* They are non-narcotic drug.
* They don't cause physical dependence or addiction.
* They don't depress CNS.
* They act by inhibiting COX (Cyclooxygenase) enzyme.

IPS OWN PAPA

Date: _____ Page: _____

Classification (NSAIDs)

Nsai= narcotic analgesics or anti-inflammatory drugs are classified as follows-

1- Non-selective cox inhibitors →

(a) Salicylates → Aspirin, sodium salicylate,

(b) Indole derivative → Indomethacin, sulindac.

(c) Propionic acid derivative → ketoprofen, Ibuprofen, Naproxen

(d) Oxicam derivative → Piroxicam

(e) Pyrrole-pyrrole derivative → ketorolac

(f) Anthranilic acid derivative → Mephanamic acid

(g) Pyrazolone derivative → Phenylbutazone

(h) Aryl acetic acid derivative → Diclofenac, Acedofenac

2- Preferential COX_2 Inhibitor →

Nimesulide, Meloxicam.

3- Selective COX_2 Inhibitor →

Celecoxib, Etoricoxib, Parecoxib.

4- Analgesic - Antipyretics with poor antiinflammatory action →

Paracetamol, Nefopam, Metamizole.

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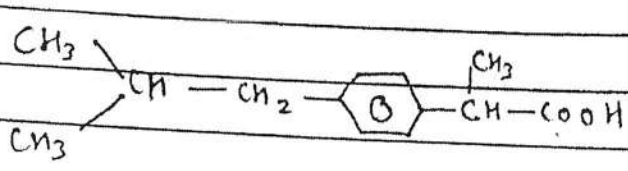
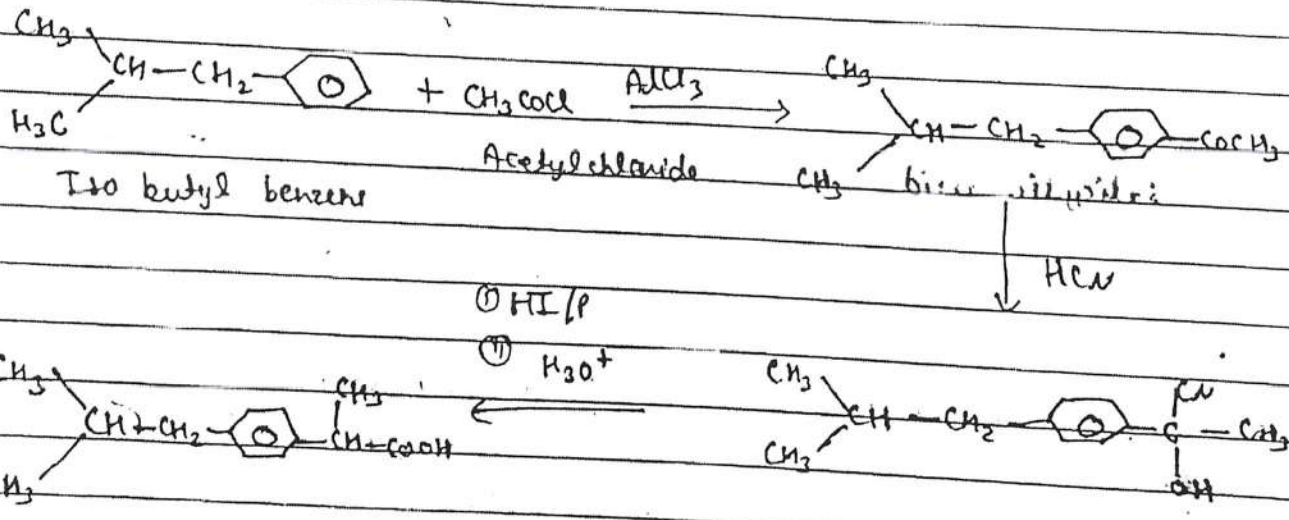
Ibuprofen

Str -1



Syn -1



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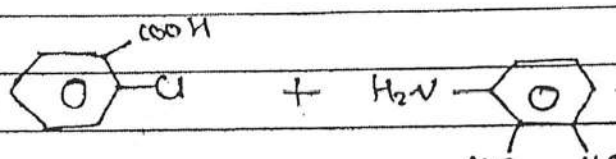
Mefenamic acid

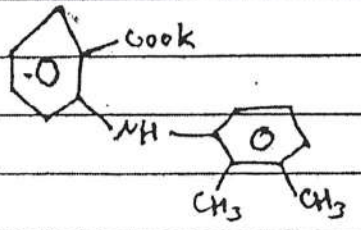
Str →

Syn →



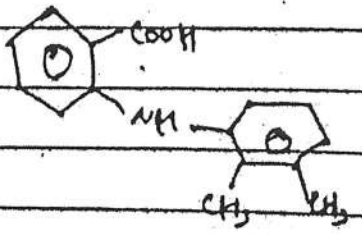
o-chloro benzoic acid 2,3 xylidene

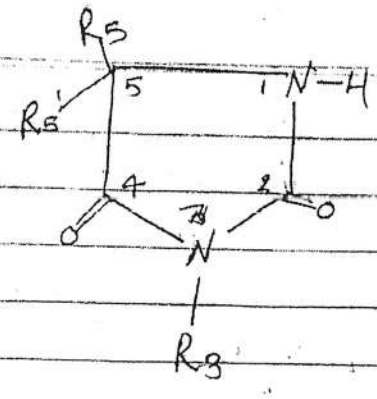
K_2CO_3

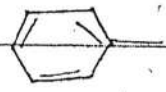
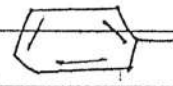
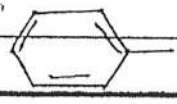
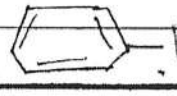


potassium salt of mefenamic acid

HCl





Hydatoin	Substitution		
	R_5	R'_5	R_3
Phenytoin			H
Mephenytoin		CH_3-CH_2-	CH_3-
Ethotoin		H	CH_3-CH_2-

[A] **Phenytoin** - Phenytoin is chemically, 5-5 diphenyl imidazolidine - 2,4- dione.

Uses - Phenytoin is an anticonvulsant that is used to treat a wide variety of seizures.

It is useful against all types of seizures except absence seizures.

It is also as an anti-arrhythmic and muscle relaxant.

[B] **Mephenytoin** - Mephenytoin is chemically, 5-ethyl-3-methyl-5-phenylimidazoline 2-4, dione.

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Page

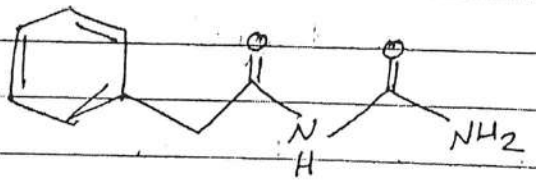
Uses - It is more active against partial and generalized tonic - clonic seizures.

The adverse effect such as dermatitis, hepatic associated with mephenytoin is higher than phenytoin.

[c] Ethotoin - Ethotoin is chemically 3-ethyl-5-phenylimidazaline 2-4-dione.

It has similar mechanism of action as that of phenytoin.

[d] Phenacemide



- Phenacemide is chemically, N-carbamoyl-2-phenylacetamide.
- It acts on the CNS to reduce the no. of and severity of seizures.
- It blocks neuronal depolarization and hypersynchronization.

Uses - Used to control certain seizures in treatment of epilepsy.

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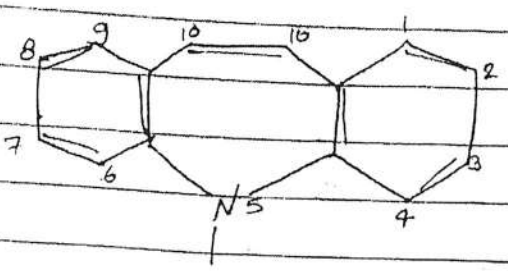
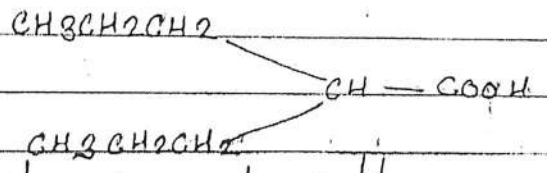
[B] Carbamazepine



Carbamazepine is chemically 5H - dibenz [b.f] azepine - 5- carbaxamide.

Uses - Carbamazepine is used as an anticonvulsan to control grand mal and psychomotor or focal seizures.

V. most Valproic Acid



- Valproic acid is chemically . 2 - propylpentanoic acid.
- It is synthetic derivative of propylpentanoic acid

Uses - Valproic acid has anticonvulsant properties and is used in the treatment of grand mal epilepsy petil mal epilepsy and complex partial seizure.
- It is also used as a mood stabilizer

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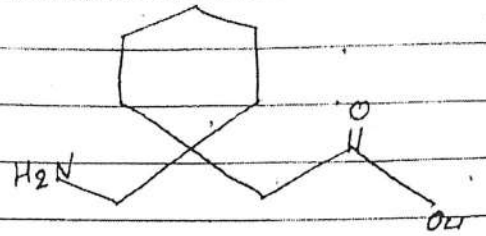
IMP Gabapentin drug



- Gabapentin is chemically, 1-(aminomethyl) cyclohexan acetic acid.
- It is synthetic GABA-mimetic analogue capable of penetrating the CNS.
- It is a water soluble amino acid, act by altering the metabolism or release of GABA and treat CNS disorganized electrical activity.
- It also acts by binding with calcium channels

Use - • Gabapentin is used in refractory partial seizures and generalized tonic-clonic seizures.

- It also approved for the treatment of ~~pethe~~ postherpetic neuralgia.

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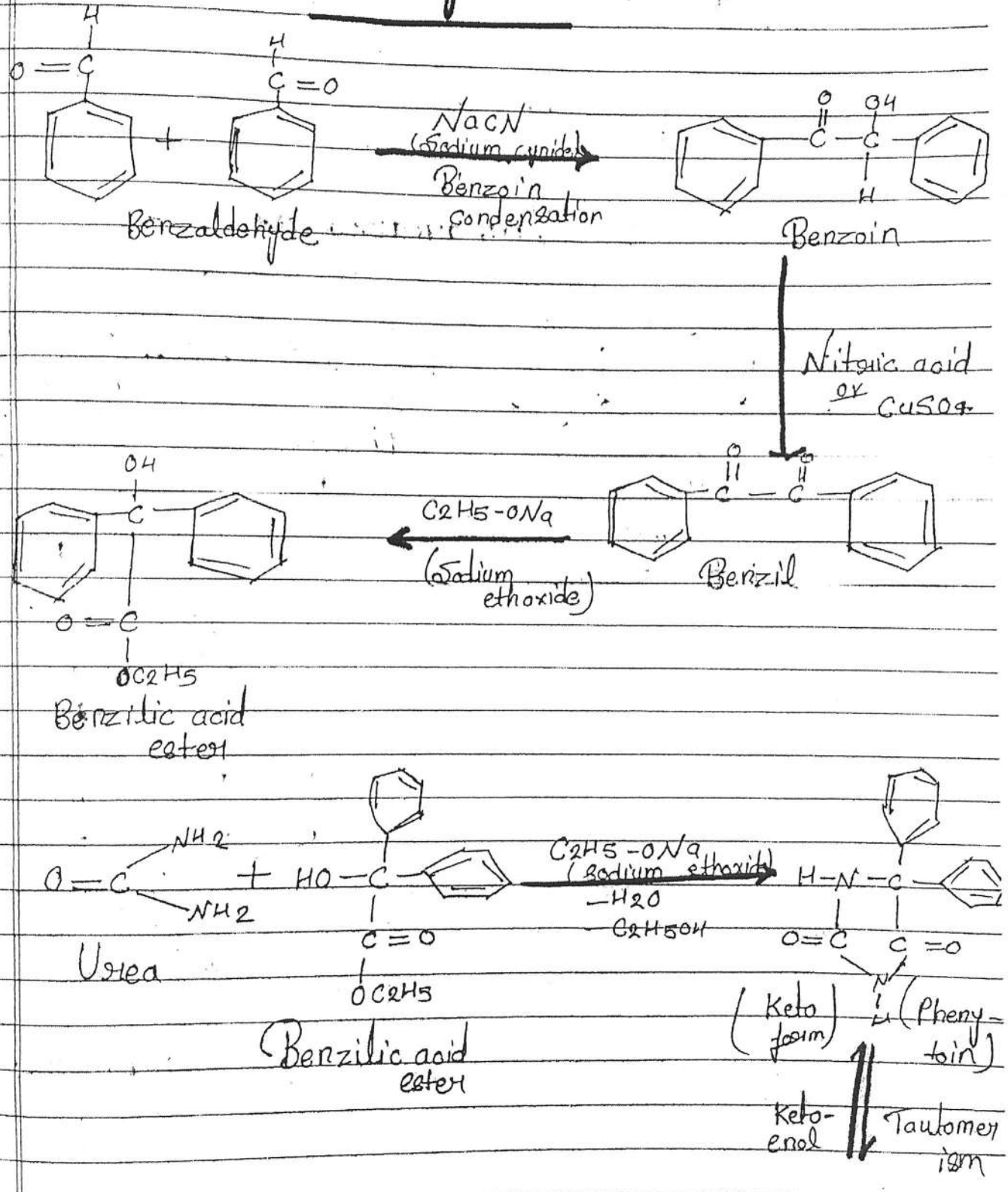
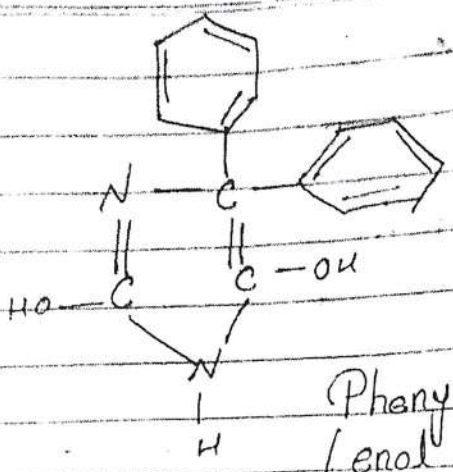
Synthesis

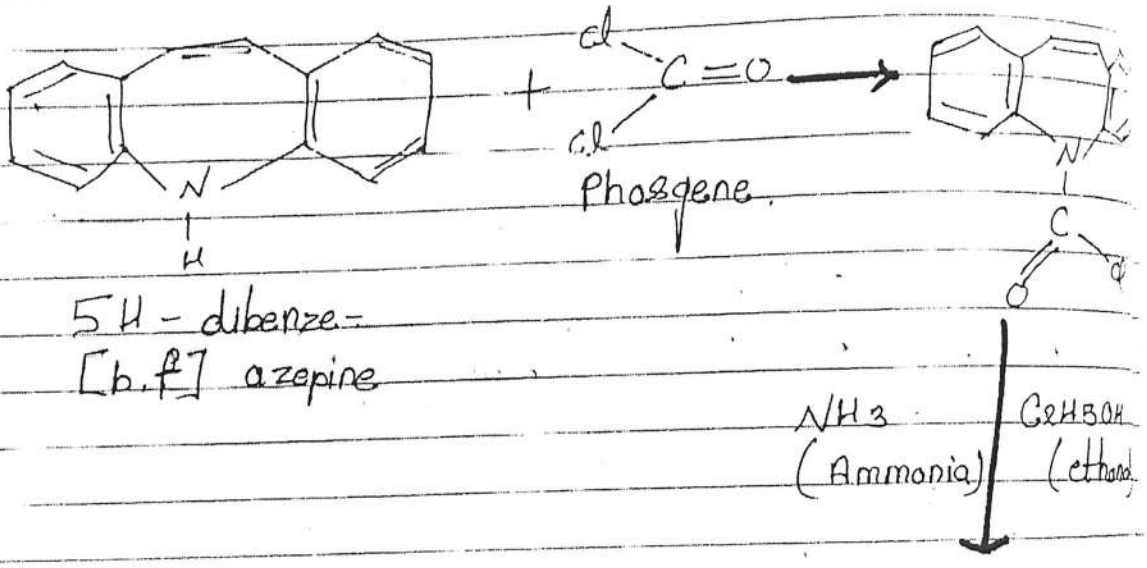
1. Phenytoin





Phenytoin
(enol form).

2. Carbamazepine



Carbamazepine

Date / /

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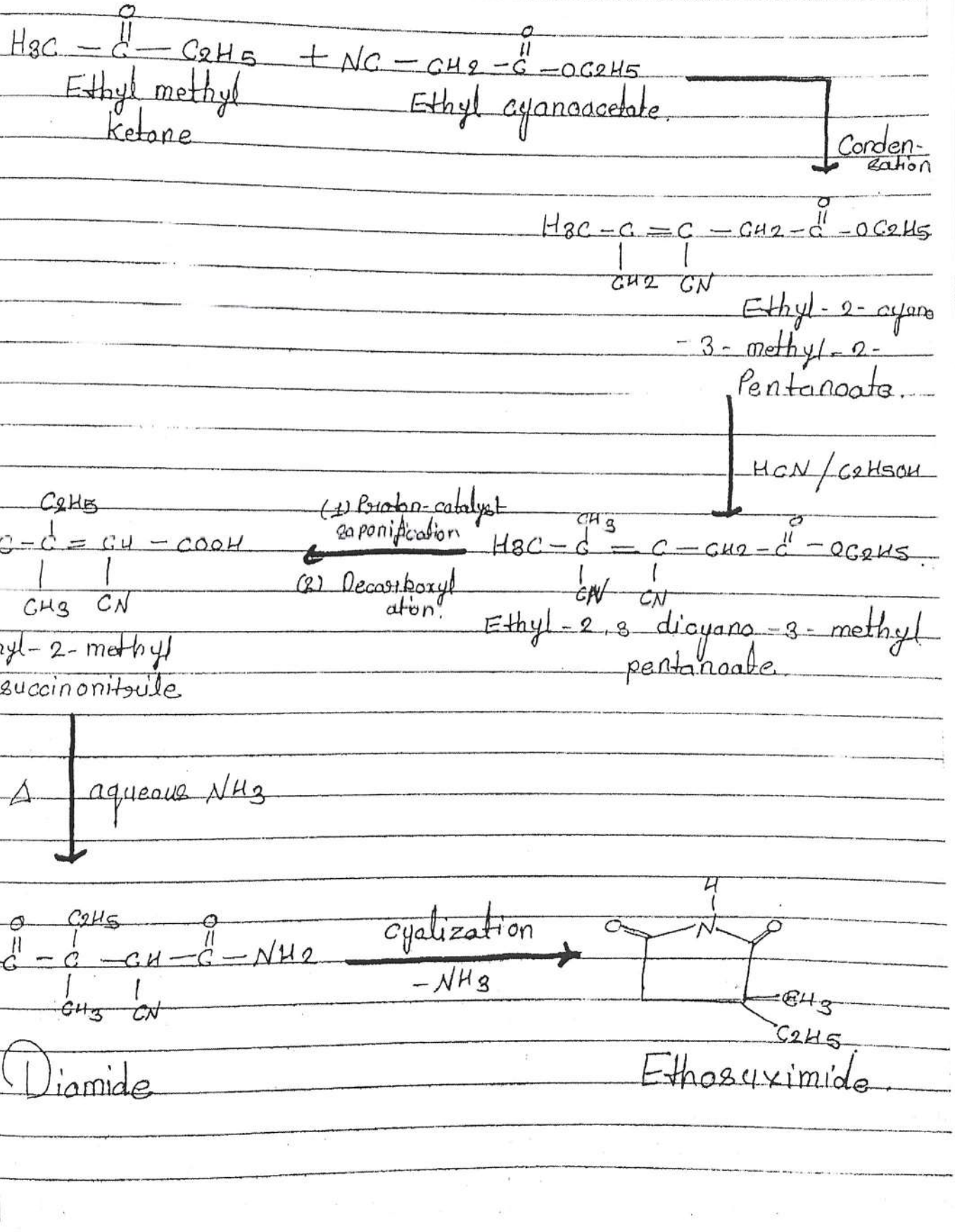
3. Ethosuximide



ST.PAULS COLLEGE OF PHARMACY

B.PHARMACY ____2____ YEAR__IV____SEM

SUBJECT NAME: MEDICINAL CHEMISTRY-I

STUDENT NAME: G. MANASA

HALL TICKET NO: 256518881020

ASSIGNMENT TOPIC	CO's	BLOOMS TAXONOMY LEVEL
1. Define solubility, Lipophilicity, Surface activity.	1	1
2. Discuss factors effecting Biotransformation.	1	2
3. Justify Phase-I reactions of Biotransformation.	1	5
4. Describe Bio-Isosterism and and give its applications	2	2

REFERENCE:

1. Foye's Principles of Medicinal Chemistry
2. Wilson and Giswold's Organic medicinal and Pharmaceutical Chemistry.
3. Burger's Medicinal Chemistry, Vol I to IV.

Submitted to : Mrs.J.Sujatha

St. Pauls College of Pharmacy.

Name : G. Manasa

Rollno : 256518881020

Class : B-Pharmacy.

Subject : Medicinal chemistry - I

Topic :- Assignment

* Define solubility, Lipophilicity, Surface activity
* Discus factors effecting Biotransformation.
* Justify phase-1 reactions of Biotransformation
* Describe Bio-Isosterism and give its application.

Submitted to :- Mrs. Sujatha Madam.

10. Define solubility, Lipophilicity, surface activity

Ans Solubility :-

Definition : The maximum amount of solute that can be dissolved in a given amount of solvent

→ Usually a limit to the solubility of one substance in another

Exceptions :- gases are always soluble in each other

→ two liquids that are mutually soluble are said to be miscible.

- alcohol and water are miscible
- oil and water are immiscible.

Example :-

Solute State	Solvent state	Example
solid	liquid	salt in water
gas	liquid	carbon dioxide in water

Lipophilicity :-

It is most important physical property of a drug in relation to its absorption, distribution potency and elimination

Lipophilicity of is often an important factor in all of the following, which include both biological and physicochemical properties

Partition coefficient is used along with another parameter to represent lipophilicity

Partition coefficient is used for the whole molecule while is related to substituted groups.

Examples :-

Hexane or toluene These non polar solvents are themselves lipophilic [Translated as "fat-loving" or "fat-liking"] the axiom that dissolves

Surface activity

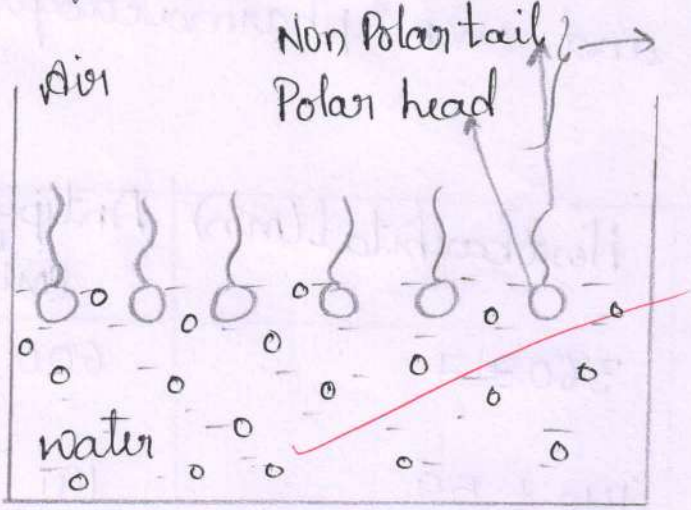
Surfactant is defined as a material that can reduce the surface tension of water at very low concentration

Surface active agents affects the drug absorption which depends on :

The chemical nature of surfactant
Its concentration
Its affects on biological membrane and the micelle formation

In lower concentration of surfactant enhanced the rate of absorption because amphiphilies reduces the surface tension and better absorption

In higher concentration of surfactant reduced the rate of absorption



Example:-

* Soap and detergents

2Q Discuss the factors effecting Biotransformation

Ans: Factors affecting drug metabolism:-

Amongst the factors which have been identified as resulting in metabolic variations are genetic, physiological, pharmaceutical factors and drug interactions.

a) Genetic factors :-

Different species and different strains within a given species, may possess different populations of enzymes which can lead to both quantitative and qualitative differences in metabolism, and even pharmacological activity

Example :-

	Animal Species	Hexobarbital (min)	Antipyrine (min)	Isoniazid (hr)
1.	Humans	360 ± 7	600	4
2.	Rat	140 ± 59	141	0.4

b) Physiologic factors :-

An individuals metabolising enzymes donot function at full efficiency for the whole of his / her life. in particular, efficiency is relati

-rely impaired in both the very young and the very old, and drug action in these subjects can be appreciably prolonged.

In view of the role played by the liver, disease can cause significant changes in drug metabolism, where as kidney disease hampers the excretion of drugs.

In case of acute viral hepatitis the half life of diazepam, meperidine and pentobarbital are decreased.

The sex of the animal may also affect the metabolism of drugs, for example, young males are more prone to sedation from barbiturates than females.

In pregnancy, barbiturates and benzodiazepines administered to mothers during child birth have also been found to pass through the placenta into the neo-born babies.

c) Pharmacodynamic factors :-

The dose, the route and the frequency of administration of drugs can affect their

metabolic profiles. the effect of protein binding also influences the metabolism.

d) Drug interaction :-

Certain drugs may stimulate or inhibit the metabolism of other drugs. for example, phenobarbital stimulates the metabolism of diphenyl-hydantoin.

more drugs compete for the xenobiotic-metabolizing enzymes are consequently inhibits the biotransformations of others. The half-life of chloropropamide.

plasma concentration of anticoagulants such as warfarin are reduced by stimultaneous application of barbiturates.

e) Environmental factors :-

Diet can influence metabolism. Starvation can deplete glycine stores and alter glycine conjugation

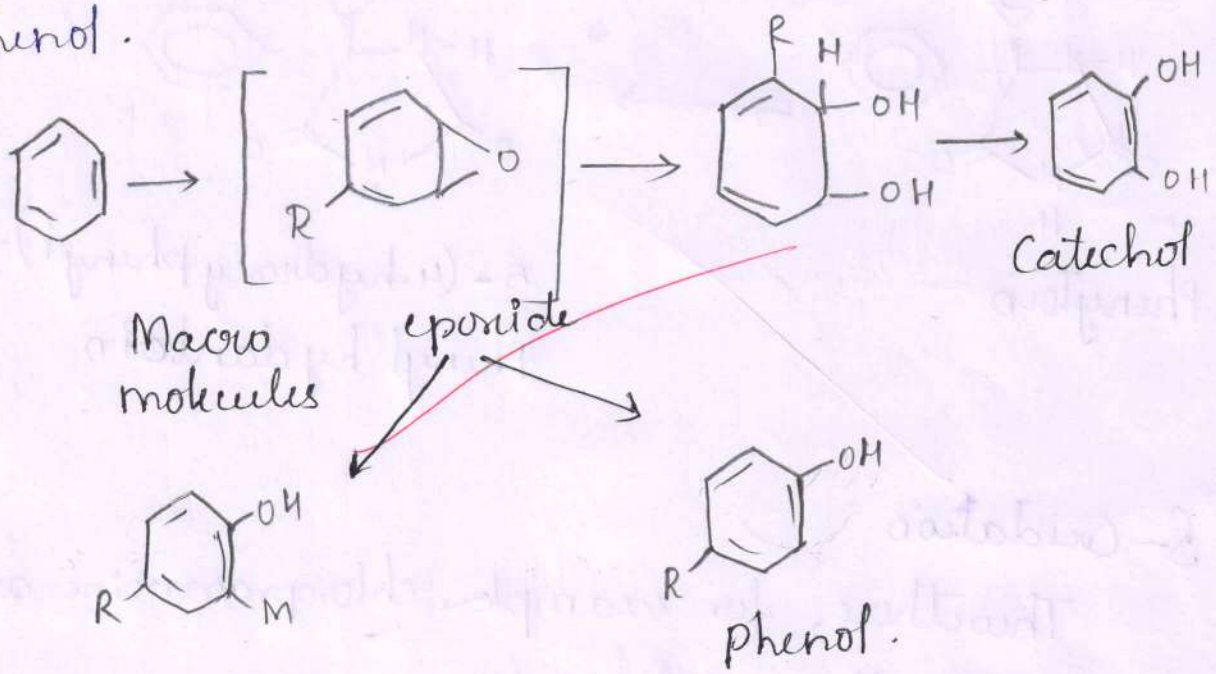
In rats and mice, the rate of hepatic metabolism of some drugs follows a diurnal rhythm. This may be true in humans aswell

3 Justify Phase-I reactions of Biotransformation

Ans: Phase-I [Functionalization]

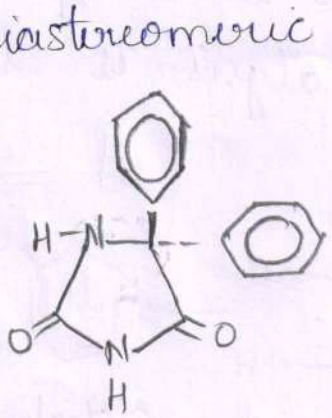
Oxidation :-

i) Aromatic hydrocarbons: The oxidation of aromatic rings occurs through a reactive epoxide (arene oxide) which can be either hydrolysed by epoxide hydrolase to a dihydrodiol or rearranged under proton catalysis to the phenol.



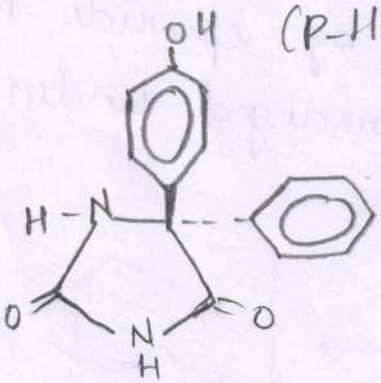
In this oxidations there is certain amount of regioselectively as there is prepondrance of levorotatory enantiomer over the diastereomer. It is thus the Pro-S-phenyl ring which is preferably

Para-hydroxylated in human. Regiochemistry of the oxidation of nifedipine by cytochrome P-450 nt is indicated by the arrow. The rat liver enzymes have been found to hydroxylate both the 2R and 2S enantiomers of the β1-selective adrenergic antagonist metaprolol at the HR-position of the prochiral 1-methylene group to give predominantly the (1R-2R) and (1R-2S) - diastereomeric products



Phenytoin

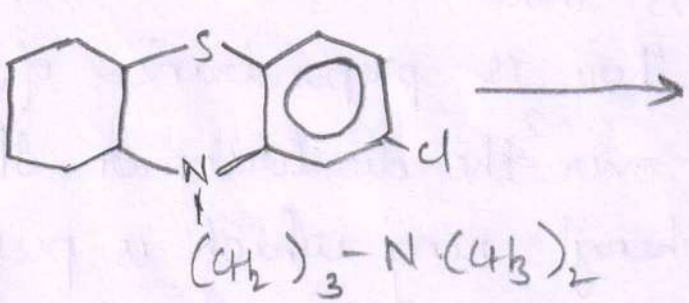
OH (P-Hydroxylation)



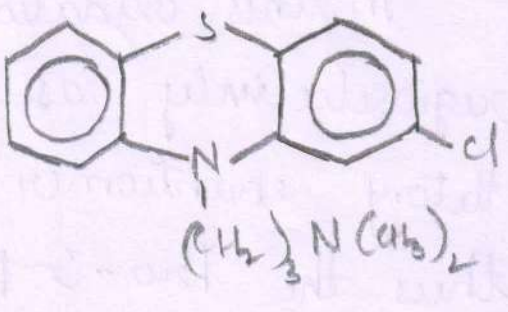
5-(4-hydroxyphenyl)-5-Phenyl hydantoin

S-Oxidation

Thioethers, for example, chloropromazine are oxidized to their sulphoxides.



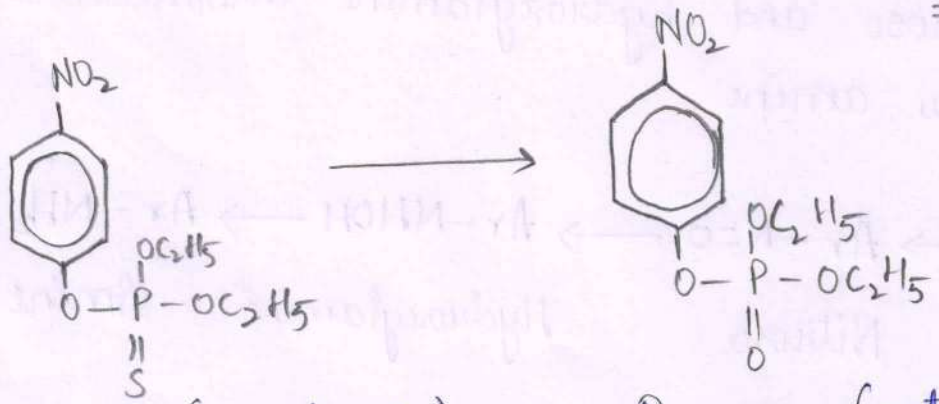
$(CH_2)_3-N(CH_3)_2$



$(CH_2)_3N(CH_3)_2$

Example:-

Conversion of thione to oxo groups.



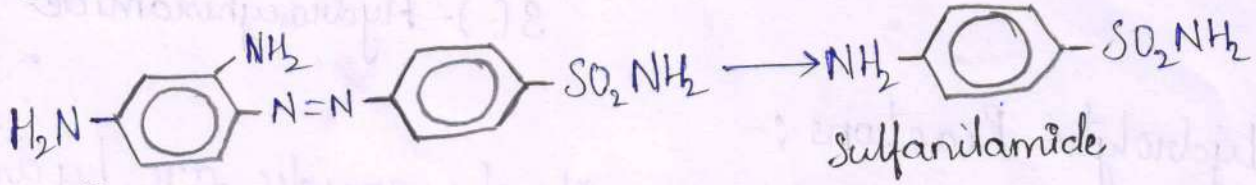
Parathion (Insecticide) Paraoxon (active agent)

Reduction:-

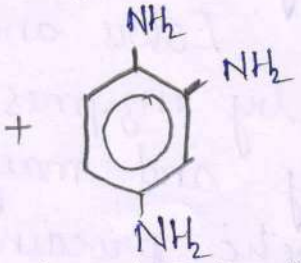
Nitro-, azo-, and carbonyl groups are subject to reduction, resulting in the formation of more polar hydroxy and amino groups. There are several reduc-tases in the liver, which depend upon NADH or NAD-PH, that catalyze such reactions

Azo reduction:-

It is believed to proceed via a hydrazo intermedi-ate (-NH-NH)



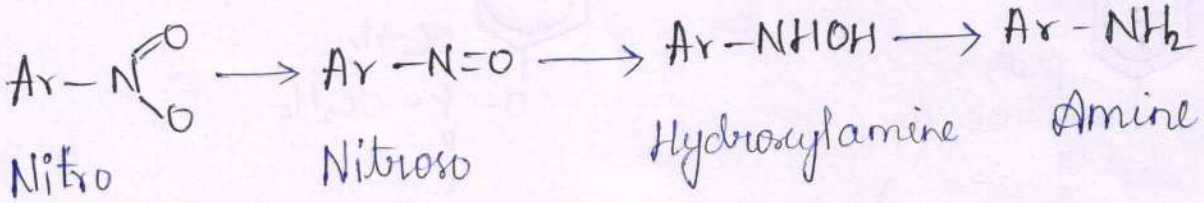
Prontosil rubrum Sulfanilamide



1,2,4, Triamino benzene.

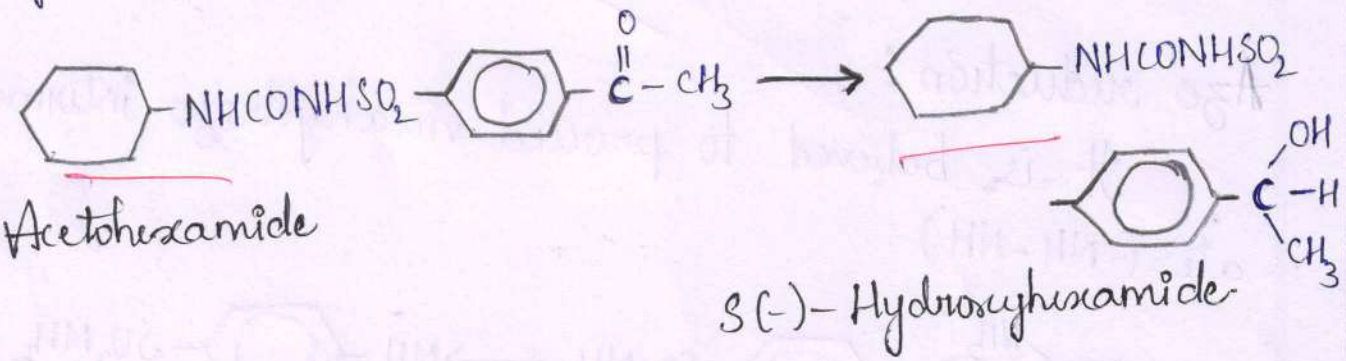
Nitro reduction:-

Aromatic nitro compounds are initially reduced to the nitroso and hydroxylamine intermediate and finally to amine



Carbonyl group:-

The carbonyl group is on occasions, found in some drugs. Aldehyde and ketone functionalities are often involved as intermediates in the metabolism of amino derivatives. Acetohexamide can give rise to hydroxyhexamide



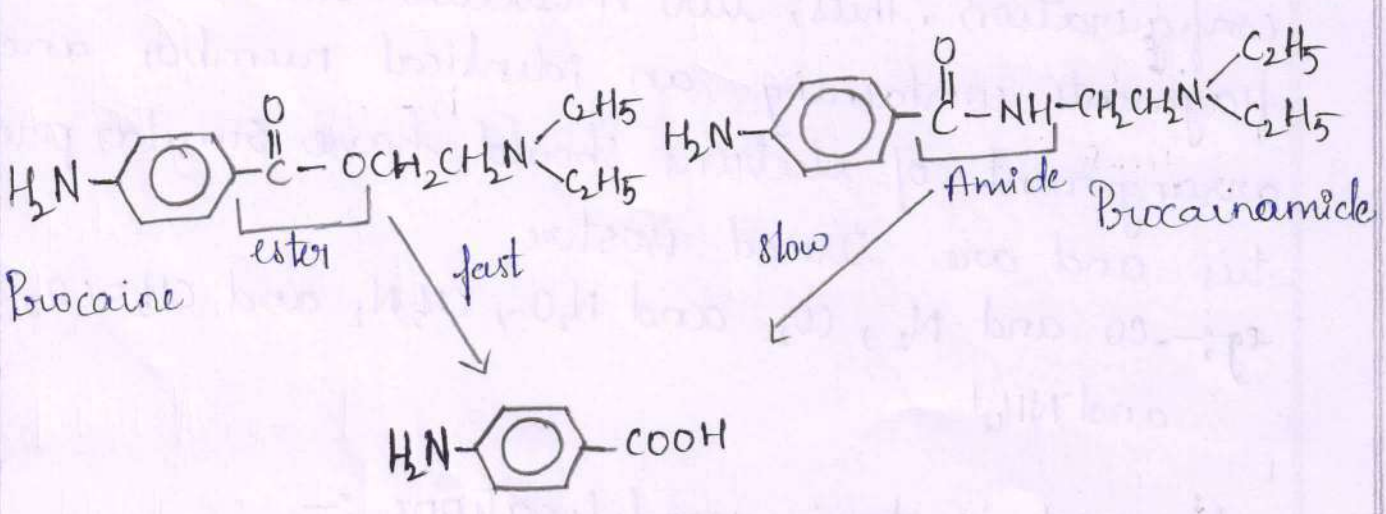
Acetohexamide

S(-)-Hydroxyhexamide

Hydrolytic Reactions:-

Esters and more slowly amides are hydroly-sed by enzymes in the blood, liver microsomes, kidney and may other tissues. Thus, the local anesthetic procaine. which is an ester, is rapidly

inactivated by plasma cholinesterase, whereas its amide analogue, procainamide is not attacked by this enzyme and is thus suitable for systemic use as an antidysrhythemic drug.



4. Describe Bio-Isosterism and give its applications.

Ans:- Bio-Isosterism :-

The discovery of a compound with promising medicinal activity leads to a search for other structurally closely related compounds, which have improved therapeutic and reduced unwanted side-effects. Much of this search has been based on isosteric relationships. In its simple form, isosteric modification involves the replacements of an atom, or group of atoms, in a molecule by another group with similar electronic and steric configuration

Isosterism is an attempt to apply to molecules or molecular fragements the promise that similarities in properties of elements within vertical groups of the Periodic table are due to identical valence electronic configuration. Thus, two molecules or molecular fragments containing an identical number and arrangement of electrons should have similar properties and are termed isostere

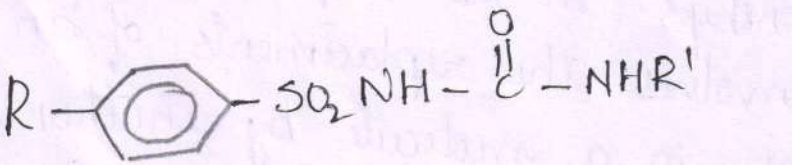
eg:- CO and N_2, CO_2 and N_2O, CH_2N_2 and $CH_2{=}CO$, CH_4 and NH_4^+

Classical isosteric modifications :-

classical bioisostere have similarities of shape and electronic configuration of atoms, groups and molecules, which they replace

i) Replacement of univalent atoms or groups:-

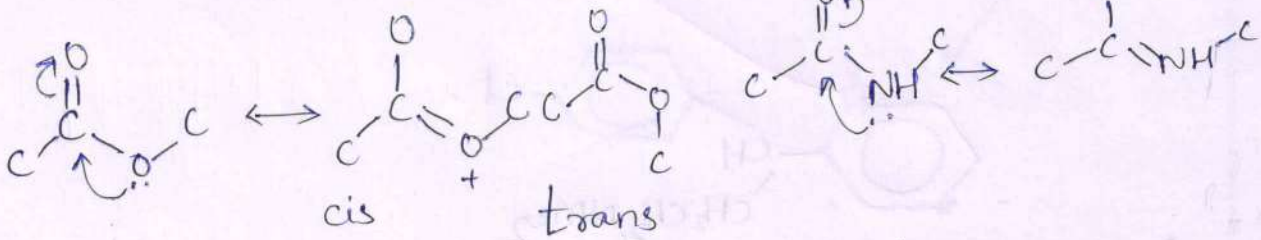
The analogous groups considered here -F(Cl), $-OH_3$ $-NH_2$ and CH_3. Programme modification of the oral hypoglycemics have involved the successive replacement of the amino ($-NH_2$) group or chlorine -Cl, to give tolbutamide and chloropripamide respectively. which possess extended biological half-lives and reduced toxicity



ii) Interchange of divalent atoms & groups :-

Bio-isosterism occurs more frequently between divalent atoms and groups. Steric similarities here are aided by similarities in bond angles, so that attached groups are specially oriented in a like manner. This is borne out in the isomeric relationship of esters and amides in esters the rotation of C-O-C bonds is restricted by resonance and aliphatic esters exist, Predominantly in the cis-configuration rather than the trans.

Group	O	S	NH	$-CH_2-$
Bond Angles	108 ± 3	112 ± 2	111 ± 3	111.5 ± 3

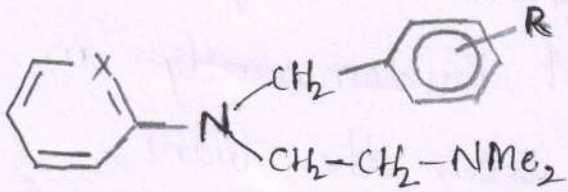


cis trans

iii) Interchange of trivalent atoms and groups

The substitution of -CH= by -N= aromatic rings has been one of the most successful application of classical isosterism. one of the most potent antihista-mines, mepyramine, has evolved from the replacement of a phenyl group in antegran by pyridyl The π electrons deficiency of the pyridine nucleus enables

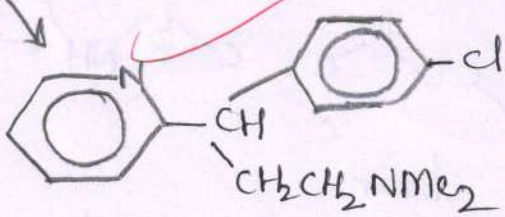
the nitrogen electron pair to hydrogen bond with a water molecule affecting an increase in hydrophillicity which is significant in determining the high level of biological activity. Substitution of the pyridinyl amino -N= by -CH= in mepyramine produces chlorpheniramine, valued for its short, powerful action and relative freedom from sedation, which is an undesirable side effect of antihistaminic drugs.



Antegran: X = CH, R = H (36.52)

Mepygramine X = N R = O.Me (P) (36.53)

chlorpheniramin X = N R = cl (P). (36.54)

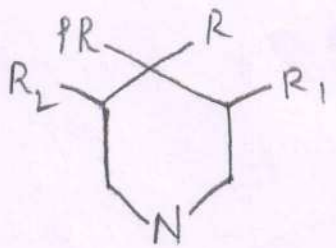


Non-classical isosteres:- They donot obey the steric and electronic definition of classial isosteres Also they do not have the same number of atoms as a replacement

—CO—	—COOH	$-SO_2NH_2$	H	—CH
$-SO_2-$	$-SO_3H$	$-PO(OH)NH_2$	F	—NH.
Annuler	—O—C—		open	—C—O—

Non-classical isosteric modification :- Those that substituted in a certain molecule, give origin to a component where steric arrangement and electronic configuration are similar to those of the parent compound Examples of pairs of isosteres are:- H and F, CO and SO_2, SO_2NH_2 and $-PO(OH)NH_2$

i) Reversal of groups :- Trimaperidine is the propanoate ester of a piperidyl alcohol, whilst pethidine, meperidine, is an ethyl ester of a piperidyl carboxylic acid. Thus the first compound is related to the second by reversal of an ester group.



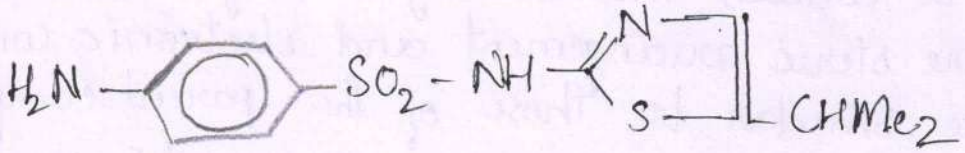
Trimaperidine : R = O, COEt R1 = R2 = Me (36.55)

Pethidine : R = COOEt R1 = R2 = Me (36.56)

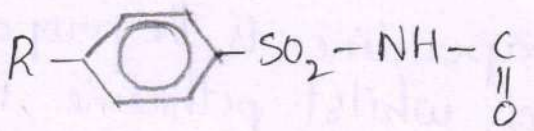
ii) Ring opening and closure :-

Sulphathiazole derivative (36.57) lowered the blood sugar almost to a fatal level. Sulphonamide oral hypoglycemic agents arose based on this observation. Modification opening of the thiazole ring to give a thiourea unit in which =S was ultimately replaced by =O yielded carbutamide (36.58) which was later replaced by the less

Toxic tolbutamide (36.59)



36.57



$R = NH_2$ carbutamide (36.58); $R = CH_3$ tolbutamide (36.59)

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

43 responses

Accepting responses

Summary Question Individual

reyankhan642@gmail.com < 2 of 43 >

24 of 30 points *Score released Dec 10 10:41 AM* Release score

St.Pauls College of Pharmacy B.pharm IV sem sec-A II sessional examination (2019-2020)

Medicinal chemistry- BP402T
Time 30 mins, after 30 mins exam can not be submitted

* Required

Email *

kutubuddinsk2001@gmail.com

Name of the student(as per the college records) * / 0

Kutubuddin Sk

Add individual feedback

Hall Ticket No. in full 2565188810 * / 0

256518881037

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Serine ✓

c. Phenylalanina

d. Alaninc

Add individual feedback

✓ 2. Uptake of acetyl choline is inhibited by_____ * 1 / 1

a. Hemicholinium ✓

b. Choline

c.Denosyl methionine

d. Acetyl coA

Add individual feedback

✗ 3. In acetyl choline the nitrogen atom was replaced by arsenic, phosphorus or sulphur. * / 1

a. Less active ✗

b. More active

c. A and B

d. None of the above

No correct answers

Add individual feedback

✓ 4. Acetyl cholinesterase inhibitors example * 1 / 1

a. Methacholine

b. Carbacol

c. Pilocarpine

d. Physostigmine ✓

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Decreased conduction velocity

c. Decreased ventricular contractility

d. All the above ✓

Add individual feedback

✓ 6. Effects of muscarinic agonists on the gastrointestinal tract * 1 / 1

a. Reduced intestinal peristalsis

b. Reduced smooth muscle tone

c. Reduced contraction amplitude

d. None of the above ✓

Add individual feedback

✓ 7. In acetyl choline substitution of the beta-hydrogen of ethylene bridge by alkyl groups makes the drug * 1 / 1

a. More active

b. Less active ✓

c. Inactive

d. None of the above

Add individual feedback

✓ 8. The mechanism of the parasympathomimetic effect of physostigmine * 1 / 1

a. Increase action of acetyl cholinesterase

b. Inhibition of acetyl cholinesterase ✓

c. No action on acetyl cholinesterase

d. None of the above

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

a. Decreased contractions of smooth muscle of GIT

b. Decreased contractions of smooth muscle of urinary tract

c. Dilation of pupils

d. All the above ✓

Add individual feedback

✓ 10. Examples of barbiturates * 1 / 1

a. Estazolam

b. Zolpidem.

c. Pentobarbital ✓

d. Doxylamine

Add individual feedback

✓ 11. The nucleus involved in the structure of Zolpidem tartrate 1 / 1

a. Pyrazolopyrimidine

b. Cyclopyrroline

c. Imidazopyridine ✓

d. Benzodiazapine

Add individual feedback

✓ 12. Mechanism of action of Barbiturates * 1 / 1

a. Enhance GABA inhibitory response. ✓

b. Decrease GABA inhibitory response

c. a and b

d. None of the above

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. influenses water solubility

both a and b

none of the above

Correct answer

a. influeses the lipid solubility

Add individual feedback

✓ 14. substitutiom of N1 and N3 amide hydrogen by alkyl groups in barbiturates * 1 / 1

a. Inactive ✓

b. More active

c. Less active

d. None of the bove

Add individual feedback

✓ 15. Most common receptor for anti psychotics * 1 / 1

a. D1

b.D2 ✓

c.D3

d.D4

Add individual feedback

✓ 16. Drug causing agranulocytosis * 1 / 1

a. Pimozide

b. Clozapine ✓

c. Risperidone

c. Olanzapine

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Increases neuroleptic potency

c. a and b

d. None of the above

Add individual feedback

18. Anti-psychotic drugs with least extra pyramidal side effects. * 0 / 1

a. Triflupromazine

b. Thioridazine

c. Pimozide

d. Trifluperazine

Correct answer

b. Thioridazine

Add individual feedback

19. Antipsychotic drug is * 0 / 1

a. Doxepine

b. Fluoxetine

c.Cloxapine

d. All

Correct answer

b. Fluoxetine

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b.Glutamate

c. Dopamine ✓

d. Nicotinic

Add individual feedback

✓ 21. Drugs used for Alzheimer's disease acting on NMDA receptor is * 1 / 1

a. Donepezil

b. Memantine ✓

c. Tacrine

d. Galantamine

Add individual feedback

✓ 22. The following drug is Iminostilbenes * 1 / 1

a. Clonazepam

b.Diazepam

c. Carbamazepine ✓

d. Phenytoin

Add individual feedback

✗ 23. Valproic acid acts by _ * 0 / 1

a. Inhibits GABA transaminase

b. Increase GABA activity ✗

c. a and b

d. None of the above

Correct answer

c. a and b

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Progabide

c. Ethosuccimide

d. Mephobarbital

Add individual feedback

✗ 25. Starting material for the synthesis of Carbamazepine * 0 / 1

a. 2-Nitro benzylchloride

b. Benzophenone

c. 4-Ethyl methyl pyrrolidine

d. 2-Hydroxy imino stilbene ✗

Correct answer

a. 2-Nitro benzylchloride

Add individual feedback

✓ 26. In benzodiazepam structure addition of electron withdrawing group to Ring A gives * 1 / 1

a. More active compounds ✓

b. Less active compounds

c. Inactive compounds

d. None of the above

Add individual feedback

✓ 27. Ultra short acting barbiturate drug example * 1 / 1

a. Thiopentone ✓

b. phenobarbitone

c. Pentobarbitone

d. Butobarbitone

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Anti arrhythmic

c. Insomnia ✓

d. Anti hypertensive

Add individual feedback

✓ 29. Starting material for the synthesis of Ketamine * 1 / 1

a. O-Chloro benznitrile ✓

b. 2-Chloro trifluoro ethyl methyl ether

c. P-nitro benzoic acid

d. None of the above

Add individual feedback

✓ 30. Example for Inhalational halogenated anesthetic * 1 / 1

a. ketamine

b. Morphine

c. Halothane ✓

d. Barbiturate

Add individual feedback

Submitted 7/28/20, 10:06 AM

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

43 responses

Accepting responses

Summary Question Individual

taslimali291@gmail.com < 14 of 43 >

19 of 30 points *Score released Dec 10 10:41 AM* Release score

St.Pauls College of Pharmacy B.pharm IV sem sec-A II sessional examination (2019-2020)

Medicinal chemistry- BP402T
Time 30 mins, after 30 mins exam can not be submitted

* Required

Email *

taslimali291@gmail.com

Name of the student(as per the college records) * / 0

Md Taslim

Add individual feedback

Hall Ticket No. in full 2565188810 * / 0

256518881050

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Serine ✓

c. Phenylalanina

d. Alanine

Add individual feedback

✗ 2. Uptake of acetyl choline is inhibited by_____ * 0 / 1

a. Hemicholinium

b. Choline ✗

c.Denosyl methionine

d. Acetyl coA

Correct answer

a. Hemicholinium

Add individual feedback

✗ 3. In acetyl choline the nitrogen atom was replaced by arsenic, phosphorus or sulphur. * / 1

a. Less active ✗

b. More active

c. A and B

d. None of the above

No correct answers

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Carbacol

c. Pilocarpine

d. Physostigmine ✓

Add individual feedback

✓ 5. Cardiac muscarinic M2 receptor effects: * 1 / 1

a. Decreased atrial contractility

b. Decreased conduction velocity

c. Decreased ventricular contractility

d. All the above ✓

Add individual feedback

✓ 6. Effects of muscarinic agonists on the gastrointestinal tract * 1 / 1

a. Reduced intestinal peristalsis

b. Reduced smooth muscle tone

c. Reduced contraction amplitude

d. None of the above ✓

Add individual feedback

✗ 7. In acetyl choline substitution of the beta-hydrogen of ethylene bridge by alkyl groups makes the drug * 0 / 1

a. More active

b. Less active

c. Inactive ✗

d. None of the above

Correct answer

b. Less active

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Inhibition of acetyl cholinesterase

c. No action on acetyl cholinesterase

d. None of the above

Correct answer

b. Inhibition of acetyl cholinesterase

Add individual feedback

✗ 9. Muscarinic antagonists applications are * 0 / 1

a. Decreased contractions of smooth muscle of GIT ✗

b. Decreased contractions of smooth muscle of urinary tract

c. Dilation of pupils

d. All the above

Correct answer

d. All the above

Add individual feedback

✓ 10. Examples of barbiturates * 1 / 1

a. Estazolam

b. Zolpidem.

c. Pentobarbital ✓

d. Doxylamine

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings

Total points: 30

b. Cyclopyrroline

c. Imidazopyridine ✓

d. Benzodiazapine

Add individual feedback

✓ 12. Mechanism of action of Barbiturates * 1 / 1

a. Enhance GABA inhibitory response. ✓

b. Decrease GABA inhibitory response

c. a and b

d. None of the above

Add individual feedback

✗ 13. Substitution at 5th position of Barbiturates with alkyl groups * 0 / 1

a. influeses the lipid solubility

b. influenses water solubility

both a and b

none of the above

Add individual feedback

✓ 14. substitutiom of N1 and N3 amide hydrogen by alkyl groups in barbiturates * 1 / 1

a. Inactive ✓

b. More active

c. Less active

d. None of the bove

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

a. D1

b.D2 ✓

c.D3

d.D4

Add individual feedback

✓ 16. Drug causing agranulocytosis * 1 / 1

a. Pimozide

b. Clozapine ✓

c. Risperidone

c. Olanzapine

Add individual feedback

✗ 17. Replacement of keto moiety with thioketone group in Haloperidol * 0 / 1

a. Decreases neuroleptic potency

b. Increases neuroleptic potency ✗

c. a and b

d. None of the above

Correct answer

a. Decreases neuroleptic potency

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings

Total points: 30

b. Thioridazine

c. Pimozide

d. Trifluperazine

Correct answer

b. Thioridazine

Add individual feedback

✗ 19. Antipsychotic drug is * 0 / 1

a. Doxepine

b. Fluoxetine

c.Cloxapine

d. All

Correct answer

b. Fluoxetine

Add individual feedback

✓ 20. Haloperidol acts on which receptor * 1 / 1

a. Adrenaline

b.Glutamate

c. Dopamine

d. Nicotinic

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Memantine ✓

c. Tacrine

d. Galantamine

Add individual feedback

✓ 22. The following drug is Iminostilbenes * 1 / 1

a. Clonazepam

b.Diazepam

c. Carbamazepine ✓

d. Phenytoin

Add individual feedback

✗ 23. Valproic acid acts by _ * 0 / 1

a. Inhibits GABA transaminase

b. Increase GABA activity ✗

c. a and b

d. None of the above

Correct answer

c. a and b

Add individual feedback

✓ 24. The following drug show the activity by enhancement of Na channel activation * 1 / 1

a. Phenytoin ✓

b. Progabide

c. Ethosuccimide

d. Mephobarbital

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Benzophenone

c. 4-Ethyl methyl pyrrolidine

d. 2-Hydroxy imino ctilbene

Add individual feedback

✗ 26. In benzodiazepam structure addition of electron withdrawing group to Ring A gives * 0 / 1

a. More active compounds

b. Less active compounds ✗

c. Inactive compounds

d. None of the above

Correct answer

a. More active compounds

Add individual feedback

✓ 27. Ultra short acting barbiturate drug example * 1 / 1

a. Thiopentone ✓

b. phenobarbitone

c. Pentobarbitone

d. Butobarbitone

Add individual feedback

✓ 28. Alprazolam used for the treatment of * 1 / 1

a. Analgesic

b. Anti arrhythmic

c. Insomnia ✓

d. Anti hypertensive

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. 2-Chloro trifluoro ethyl methyl ether

c. P-nitro benzoic acid

d. None of the above

Add individual feedback

✓ 30. Example for Inhalational halogenated anesthetic * 1 / 1

a. ketamine

b. Morphine

c. Halothane ✓

d. Barbiturate

Add individual feedback

Submitted 7/28/20, 10:20 AM

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

43 responses

Accepting responses

Summary Question Individual

ayeshaosma@gmail.com 41 of 43

10 of 30 points *Score released Dec 10 10:41 AM* Release score

St.Pauls College of Pharmacy B.pharm IV sem sec-A II sessional examination (2019-2020)

Medicinal chemistry- BP402T
Time 30 mins, after 30 mins exam can not be submitted

* Required

Email *

ayeshaosma@gmail.com

Name of the student(as per the college records) * / 0

Ayesha osman

Add individual feedback

Hall Ticket No. in full 2565188810 * / 0

13

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Serine

c. Phenylalanina

d. Alanine

Correct answer

b. Serine

Add individual feedback

2. Uptake of acetyl choline is inhibited by_____ * 0 / 1

a. Hemicholinium

b. Choline

c.Denosyl methionine

d. Acetyl coA

Correct answer

a. Hemicholinium

Add individual feedback

3. In acetyl choline the nitrogen atom was replaced by arsenic, phosphorus or sulphur. * / 1

a. Less active

b. More active

c. A and B

d. None of the above

No correct answers

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Carbacol

c. Pilocarpine

d. Physostigmine

Correct answer

d. Physostigmine

Add individual feedback

5. Cardiac muscarinic M2 receptor effects: * 0 / 1

a. Decreased atrial contractility

b. Decreased conduction velocity

c. Decreased ventricular contractility

d. All the above

Correct answer

d. All the above

Add individual feedback

6. Effects of muscarinic agonists on the gastrointestinal tract * 0 / 1

a. Reduced intestinal peristalsis

b. Reduced smooth muscle tone

c. Reduced contraction amplitude

d. None of the above

Correct answer

d. None of the above

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Less active

c. Inactive

d. None of the above

Correct answer

b. Less active

Add individual feedback

✗ 8. The mechanism of the parasympathomimetic effect of physostigmine * 0 / 1

a. Increase action of acetyl cholinesterase ✗

b. Inhibition of acetyl cholinesterase

c. No action on acetyl cholinesterase

d. None of the above

Correct answer

b. Inhibition of acetyl cholinesterase

Add individual feedback

✓ 9. Muscarinic antagonists applications are * 1 / 1

a. Decreased contractions of smooth muscle of GIT

b. Decreased contractions of smooth muscle of urinary tract

c. Dilation of pupils

d. All the above ✓

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Zolpidem.

c. Pentobarbital ✓

d. Doxylamine

Add individual feedback

✗ 11. The nucleus involved in the structure of Zolpidem tartrate 0 / 1

a. Pyrazolopyrimidine

b. Cyclopyrroline

c. Imidazopyridine

d. Benzodiazapine ✗

Correct answer

c. Imidazopyridine

Add individual feedback

✓ 12. Mechanism of action of Barbiturates * 1 / 1

a. Enhance GABA inhibitory response. ✓

b. Decrease GABA inhibitory response

c. a and b

d. None of the above

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. influenses water solubility

both a and b

none of the above

Correct answer

a. influeses the lipid solubility

Add individual feedback

14. substitutiom of N1 and N3 amide hydrogen by alkyl groups in barbiturates * 0 / 1

a. Inactive

b. More active

c. Less active

d. None of the bove

Correct answer

a. Inactive

Add individual feedback

15. Most common receptor for anti psychotics * 1 / 1

a. D1

b.D2

c.D3

d.D4

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

- (●) b. Clozapine ✓
- ( ) c. Risperidone
- ( ) c. Olanzapine

Add individual feedback

✗ 17. Replacement of keto moiety with thioketone group in Haloperidol * 0 / 1

- ( ) a. Decreases neuroleptic potency
- ( ) b. Increases neuroleptic potency
- (●) c. a and b ✗
- ( ) d. None of the above

Correct answer

- (●) a. Decreases neuroleptic potency

Add individual feedback

✗ 18. Anti-psychotic drugs with least extra pyramidal side effects. * 0 / 1

- ( ) a. Trifluipromazine
- ( ) b. Thioridazine
- (●) c. Pimozide ✗
- ( ) d. Trifluperazine

Correct answer

- (●) b. Thioridazine

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Fluoxetine

c.Cloxapine

d. All ✗

Correct answer

b. Fluoxetine

Add individual feedback

✓ 20. Haloperidol acts on which receptor * 1 / 1

a. Adrenaline

b.Glutamate

c. Dopamine ✓

d. Nicotinic

Add individual feedback

✗ 21. Drugs used for Alzheimer's disease acting on NMDA receptor is * 0 / 1

a. Donepezil

b. Memantine

c. Tacrine

d. Galantamine ✗

Correct answer

b. Memantine

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b.Diazepam

c. Carbamazepine ✓

d. Phenytoin

Add individual feedback

✗ 23. Valproic acid acts by _ * 0 / 1

a. Inhibits GABA transaminase

b. Increase GABA activity ✗

c. a and b

d. None of the above

Correct answer

c. a and b

Add individual feedback

✗ 24. The following drug show the activity by enhancement of Na channel activation * 0 / 1

a. Phenytoin

b. Progabide

c. Ethosuccimide

d. Mephobarbital ✗

Correct answer

a. Phenytoin

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Benzophenone ✗

c. 4-Ethyl methyl pyrrolidine

d. 2-Hydroxy imino stilbene

Correct answer

a. 2-Nitro benzylchloride

Add individual feedback

✓ 26. In benzodiazepam structure addition of electron withdrawing group to Ring A gives * 1 / 1

a. More active compounds ✓

b. Less active compounds

c. Inactive compounds

d. None of the above

Add individual feedback

✗ 27. Ultra short acting barbiturate drug example * 0 / 1

a. Thiopentone

b. phenobarbitone

c. Pentobarbitone ✗

d. Butobarbitone

Correct answer

a. Thiopentone

Add individual feedback

MC-I , sec-A II sessional examination (2019-2020)

Questions Responses 43 Settings Total points: 30

b. Anti arrhythmic

c. Insomnia ✓

d. Anti hypertensive

Add individual feedback

✗ 29. Starting material for the synthesis of Ketamine * 0 / 1

a. O-Chloro benznitrile

b. 2-Chloro trifluoro ethyl methyl ether

c. P-nitro benzoic acid

d. None of the above ✗

Correct answer

a. O-Chloro benznitrile

Add individual feedback

✓ 30. Example for Inhalational halogenated anesthetic * 1 / 1

a. ketamine

b. Morphine

c. Halothane ✓

d. Barbiturate

Add individual feedback

Submitted 7/28/20, 10:56 AM

Semester IV

Course code	Name of the course	Internal Assessment				End Semester Exams		Total Marks
		Continuous Mode	Sessional Exams		Total	Marks	Duration	
			Marks	Duration				
BP401T	Pharmaceutical Organic Chemistry III– Theory	10	15	1 Hr	25	75	3 Hrs	100
BP402T	Medicinal Chemistry I – Theory	10	15	1 Hr	25	75	3 Hrs	100
BP403T	Physical Pharmaceutics II – Theory	10	15	1 Hr	25	75	3 Hrs	100
BP404T	Pharmacology I – Theory	10	15	1 Hr	25	75	3 Hrs	100
BP405T	Pharmacognosy I – Theory	10	15	1 Hr	25	75	3 Hrs	100
BP406P	Medicinal Chemistry I – Practical	5	10	4 Hr	15	35	4 Hrs	50
BP407P	Physical Pharmaceutics II – Practical	5	10	4 Hrs	15	35	4 Hrs	50
BP408P	Pharmacology I – Practical	5	10	4 Hrs	15	35	4 Hrs	50
BP409P	Pharmacognosy I – Practical	5	10	4 Hrs	15	35	4 Hrs	50
Total		**70**	**115**	**21 Hrs**	**185**	**515**	**31 Hrs**	**700**

BP406P. MEDICINAL CHEMISTRY – I (Practical)

4 Hours/Week

I	**Preparation of drugs/ intermediates**
1	1,3-pyrazole
2	1,3-oxazole
3	Benzimidazole
4	Benztriazole
5	2,3- diphenyl quinoxaline
6	Benzocaine
7	Phenytoin
8	Phenothiazine
9	Barbiturate
II	**Assay of drugs**
1	Chlorpromazine
2	Phenobarbitone
3	Atropine
4	Ibuprofen
5	Aspirin
6	Furosemide
III	**Determination of Partition coefficient for any two drugs**

Recommended Books (Latest Editions)

1. Wilson and Giswold's Organic medicinal and Pharmaceutical Chemistry.
2. Foye's Principles of Medicinal Chemistry.
3. Burger's Medicinal Chemistry, Vol I to IV.
4. Introduction to principles of drug design- Smith and Williams.
5. Remington's Pharmaceutical Sciences.
6. Martindale's extra pharmacopoeia.

B.PHARMACY IV SEMESTER (2019-2020)

CO-PO MATRICES

Code/Sub	COURSE OUTCOMES	PO1	PO2	PO3	PO4	PO5	PO6	PO7	PO8	PO9	PO10	PO11
BP406P Medicinal Chemistry I – Practical C214	C406.1 Calculate the partition coefficient values of various medicinal compounds and correlation with the biological activity.	3	2	2							1	1
	C406.2 Understand the basic principles and reaction mechanisms involved in the synthesis of drugs.	2	1	2							1	2
	C406.3 Calculate the amount of active pharmaceutical ingredient present in the dosage form.	3	2	1							1	2
	C406.4 Apply purification techniques like recrystallisation, reflux condensation and vaccum filtration.	2	2	2								1
	C406.5 Design the scheme involved in the synthesis of intermediates.	2	1	1							1	1

St. Pauls
College of Pharmacy

B.Pharmacy IV Sem- Sec-A (2019-20)

SUB: Medicinal chemistry

S. No.	H.T.No.	Student Name	Theory	CO1,2,3								II Mid (30M)	CO1,2,3								Continous Mode			
			I Mid (30M)	Max	Min	Max./2	min/2	F.max	Fmin	Fmax60%	60% above scored		Max	Min	Max./2	min/2	F.max	Fmin	Fmax60%	60% above scored	Attend. (4M)	Acad. Actvt. (3M)	Student teacher inter. (3M)	Total (10M)
1	256517881003	KARNATAKA NAVEEN	13	30	13	15	6.5	25	14.5	15	FALSE	24	30	24	1	12	25	20	15	TRUE	3	2	3	8
2	256517881008	MALLELA HARI PRASAD	13	30	13	15	6.5	25	14.5	15	FALSE	23	30	23	1	11.5	25	19.5	15	TRUE	3	2	3	8
3	256517881027	ALIGE NITHYANANDAM	14	30	14	15	7	25	15	15	TRUE	21	30	21	1	10.5	25	18.5	15	TRUE	3	2	3	8
4	256517881040	KOSGI BAL REDDY	14	30	14	15	7	25	15	15	TRUE	23	30	23	1	11.5	25	19.5	15	TRUE	3	2	3	8
5	256518881001	A PAVAN KUMAR GOUD	22	30	22	15	11	25	21	15	TRUE	25	30	25	1	12.5	25	22.5	15	TRUE	4	3	3	10
6	256518881002	ABDULLAH QUDUS	23	30	23	15	11.5	25	20.5	15	TRUE	19	30	19	1	9.5	25	18.5	15	TRUE	3	3	2	8
7	256518881003	ABDUR RAKIB	AB	30	AB	15	0	25	8	15	FALSE	Ab	30	Ab	1	0	25	8	15	FALSE	2	3	3	8
8	256518881004	ADIPELLI SAIMEGHANA	18	30	18	15	9	25	19	15	TRUE	11	30	11	1	5.5	25	15.5	15	TRUE	4	3	3	10
9	256518881006	AHMED BIN HUSSAIN DAYANI	15	30	15	15	7.5	25	16.5	15	TRUE	20	30	20	1	10	25	19	15	TRUE	3	3	3	9
10	256518881007	AJMAL HOSSAIN	17	30	17	15	8.5	25	17.5	15	TRUE	20	30	20	1	10	25	19	15	TRUE	3	3	3	9
11	256518881008	ANAM FATIMA	23	30	23	15	11.5	25	21.5	15	TRUE	19	30	19	1	9.5	25	19.5	15	TRUE	4	3	3	10
12	256518881009	ANDUGULA RAJESHWARI	17	30	17	15	8.5	25	17.5	15	TRUE	23	30	23	1	11.5	25	20.5	15	TRUE	3	3	3	9
13	256518881010	ARIF SK	19	30	19	15	9.5	25	17.5	15	TRUE	Ab	30	Ab	1	0	25	8	15	FALSE	3	2	3	8
14	256518881011	AVURAKONDA MANOJ	13	30	13	15	6.5	25	15.5	15	TRUE	Ab	30	Ab	1	0	25	9	15	FALSE	4	3	2	9
15	256518881012	AYESHA KOUKAB	23	30	23	15	11.5	25	19.5	15	TRUE	18	30	18	1	9	25	17	15	TRUE	3	2	3	8
16	256518881013	AYESHA OSMAN	19	30	19	15	9.5	25	18.5	15	TRUE	10	30	10	1	5	25	14	15	FALSE	4	3	2	9
17	256518881015	BALGURI SAVITHA SAGAR	21	30	21	15	10.5	25	19.5	15	TRUE	20	30	20	1	10	25	19	15	TRUE	3	3	3	9
18	256518881016	BALUGURI ANALIKA	18	30	18	15	9	25	19	15	TRUE	24	30	24	1	12	25	22	15	TRUE	4	3	3	10
19	256518881017	BUSHRA SULTANA	23	30	23	15	11.5	25	21.5	15	TRUE	19	30	19	1	9.5	25	19.5	15	TRUE	4	3	3	10
20	256518881018	DEPALLY TEJASWI	22	30	22	15	11	25	20	15	TRUE	25	30	25	1	12.5	25	21.5	15	TRUE	4	2	3	9
21	256518881019	E SRIHARI	21	30	21	15	10.5	25	19.5	15	TRUE	22	30	22	1	11	25	20	15	TRUE	4	3	2	9
22	256518881020	GANGOLU MANASA	18	30	18	15	9	25	19	15	TRUE	22	30	22	1	11	25	21	15	TRUE	4	3	3	10
23	256518881021	GILKATHULA ANAND	19	30	19	15	9.5	25	18.5	15	TRUE	22	30	22	1	11	25	20	15	TRUE	3	3	3	9
24	256518881022	GUDEM VAISHNAVI	18	30	18	15	9	25	19	15	TRUE	19	30	19	1	9.5	25	19.5	15	TRUE	4	3	3	10
25	256518881023	GUNDOJU NIHARIKA	19	30	19	15	9.5	25	19.5	15	TRUE	23	30	23	1	11.5	25	21.5	15	TRUE	4	3	3	10
26	256518881024	GURLA NIKHITHA	19	30	19	15	9.5	25	18.5	15	TRUE	20	30	20	1	10	25	19	15	TRUE	4	2	3	9
27	256518881025	GURRAM MANASA	22	30	22	15	11	25	20	15	TRUE	25	30	25	1	12.5	25	21.5	15	TRUE	3	3	3	9
28	256518881027	HENA RUSKAR	18	30	18	15	9	25	18	15	TRUE	22	30	22	1	11	25	20	15	TRUE	4	2	3	9
29	256518881028	IZAZ AHAMMED	17	30	17	15	8.5	25	17.5	15	TRUE	20	30	20	1	10	25	19	15	TRUE	4	3	2	9
30	256518881029	JALAPALA SHAMBAVI	18	30	18	15	9	25	18	15	TRUE	22	30	22	1	11	25	20	15	TRUE	3	3	3	9
31	256518881030	JINNIKUNTLA SANTHOSHA	23	30	23	15	11.5	25	20.5	15	TRUE	23	30	23	1	11.5	25	20.5	15	TRUE	4	3	2	9
32	256518881031	JUVERIYA SULTANA	22	30	22	15	11	25	20	15	TRUE	25	30	25	1	12.5	25	21.5	15	TRUE	4	2	3	9
33	256518881032	KATTUKURI NIKITHA	24	30	24	15	12	25	22	15	TRUE	24	30	24	1	12	25	22	15	TRUE	4	3	3	10
34	256518881033	KETHAVATH JHANSI	18	30	18	15	9	25	19	15	TRUE	22	30	22	1	11	25	21	15	TRUE	4	3	3	10
35	256518881034	KOTTE SAIVEENA	17	30	17	15	8.5	25	17.5	15	TRUE	25	30	25	1	12.5	25	21.5	15	TRUE	3	3	3	9
36	256518881035	KUCHIPUDI DIVYA	19	30	19	15	9.5	25	18.5	15	TRUE	22	30	22	1	11	25	20	15	TRUE	4	3	2	9
37	256518881037	KUTUBUDDIN SK	19	30	19	15	9.5	25	18.5	15	TRUE	24	30	24	1	12	25	21	15	TRUE	3	3	3	9
38	256518881038	LAGALA NIVIDHA	20	30	20	15	10	25	20	15	TRUE	22	30	22	1	11	25	21	15	TRUE	4	3	3	10
39	256518881039	LAVADIYA BALAJI	19	30	19	15	9.5	25	19.5	15	TRUE	22	30	22	1	11	25	21	15	TRUE	4	3	3	10
40	256518881040	MALLOJU SHIVA KUMAR	20	30	20	15	10	25	20	15	TRUE	25	30	25	1	12.5	25	22.5	15	TRUE	4	3	3	10
41	256518881041	MANDALA SWATHI	20	30	20	15	10	25	19	15	TRUE	23	30	23	1	11.5	25	20.5	15	TRUE	4	2	3	9
42	256518881043	MANIRUL HOQUE	16	30	16	15	8	25	17	15	TRUE	20	30	20	1	10	25	19	15	TRUE	3	3	3	9
43	256518881045	MASUDUR RAHAMAN	18	30	18	15	9	25	18	15	TRUE	20	30	20	1	10	25	19	15	TRUE	3	3	3	9
44	256518881047	MD AMIR HAMZA	19	30	19	15	9.5	25	18.5	15	TRUE	22	30	22	1	11	25	20	15	TRUE	3	3	3	9
45	256518881048	MD FIZE	16	30	16	15	8	25	16	15	TRUE	11	30	11	1	5.5	25	13.5	15	FALSE	3	3	2	8
46	256518881050	MD TASLIM	16	30	16	15	8	25	18	15	TRUE	19	30	19	1	9.5	25	19.5	15	TRUE	4	3	3	10
																				41				
																				89.13043478				

43
93.47826087

co	co assessed	level	Internal 0.25 (I)	External	ex. Level	ex.0.75 (E)	Final level (I+E)
co1	93	3	0.75	68	2	1.5	2.25
co2	93	3	0.75	68	2	1.5	2.25
CO3	93	3	0.75	68	2	1.5	2.25
co4	89.13	3	0.75	68	2	1.5	2.25
co5	89.13	3	0.75	68	2	1.5	2.25
co6	89.13	3	0.75	68	2	1.5	2.25

St. Pauls College of Pharmacy

B.Pharmacy IV Sem- Sec-B (2019-20)

SUB: Medicinal chemistry-I

S. No.	H.T.No.	Student Name	Theory	CO1,2,3									CO 4,5,6								Contineous Mode			
			I Mid (30M)	Max	Min	Max./2	min/2	F max	Fmin	Fmax60%	60% above scored	II Mid (30M)	Max	Min	Max./2	min/2	F max	Fmin	Fmax60%	60% above scored	Attend. (4M)	Acad. Actvt. (3M)	Student teacher inter. (3M)	Total (10M)
1	256518881051	MD NASER	17	30	17	15	8.5	25	17.5	15	TRUE	24	30	24	15	12	25	21	15	TRUE	4	2	3	9
2	256518881052	MOHD ABDULLAH	16	30	16	15	8	25	17	15	TRUE	25	30	25	15	12.5	25	21.5	15	TRUE	3	3	3	9
3	256518881053	MOHAMMED MUSHRAF	19	30	19	15	9.5	25	13.5	15	TRUE	25	30	25	15	12.5	25	21.5	15	TRUE	4	2	3	9
4	256518881055	MOHD SHOIAB AFROSE	22	30	22	15	11	25	19	15	TRUE	25	30	25	15	12.5	25	20.5	15	TRUE	3	3	2	8
5	256518881056	MUAZZAM ALI	10	30	10	15	5	25	14	15	FALSE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
6	256518881057	MUBEENA SULTANA	19	30	19	15	9.5	25	18.5	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	4	3	2	9
7	256518881058	N SATHWIKA	23	30	23	15	11.5	25	20.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	4	2	3	9
8	256518881059	NAIK AZHARUDDIN	19	30	19	15	9.5	25	18.5	15	TRUE	22	30	22	15	11	25	20	15	TRUE	4	2	3	9
9	256518881060	NAKKILLA VENKATA BHARGAVI	25	30	25	15	12.5	25	22.5	15	TRUE	22	30	22	15	11	25	21	15	TRUE	4	3	3	10
10	256518881062	NENAVATH SARASWATHI	23	30	23	15	11.5	25	20.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
11	256518881063	OMER BIN KHALID BIN NASIR	19	30	19	15	9.5	25	17.5	15	TRUE	25	30	25	15	12.5	25	20.5	15	TRUE	3	3	2	8
12	256518881064	P LAVAN KUMAR	20	30	20	15	10	25	19	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	4	2	3	9
13	256518881065	PASUKULA SANJANA	23	30	23	15	11.5	25	20.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
14	256518881066	POGAKU RAVI TEJA	21	30	21	15	10.5	25	18.5	15	TRUE	21	30	21	15	10.5	25	18.5	15	TRUE	4	2	2	8
15	256518881067	POLISHETTY BALA ROHINI	22	30	22	15	11	25	20	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
16	256518881068	POLISHETTY RAHUL	22	30	22	15	11	25	20	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	4	2	3	9
17	256518881069	PURRE REECHA	23	30	23	15	11.5	25	20.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
18	256518881070	RAHUL MOLLA	22	30	22	15	11	25	21	15	TRUE	22	30	22	15	11	25	21	15	TRUE	4	3	3	10
19	256518881071	ROBIUL ISLAM	14	30	14	15	7	25	15	15	TRUE	22	30	22	15	11	25	19	15	TRUE	4	2	2	8
20	256518881073	SAMREEN FATIMA	25	30	25	15	12.5	25	20.5	15	TRUE	22	30	22	15	11	25	19	15	TRUE	3	3	2	8
21	256518881074	SANA BEGUM	22	30	22	15	11	25	20	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	4	2	3	9
22	256518881075	SARA FATIMA	18	30	18	15	9	25	17	15	TRUE	23	30	23	15	11.5	25	19.5	15	TRUE	3	2	3	8
23	256518881077	SHANIGARAM ANUSHA	22	30	22	15	11	25	20	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
24	256518881078	SHANIGARAM MAHESH	20	30	20	15	10	25	18	15	TRUE	21	30	21	15	10.5	25	18.5	15	TRUE	3	2	3	8
25	256518881079	SIRIPURAM SOUMYA	12	30	12	15	6	25	15	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	4	3	2	9
26	256518881080	SOHA MASI	21	30	21	15	10.5	25	19.5	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	3	3	3	9
27	256518881081	SYED FARHAN	16	30	16	15	8	25	17	15	TRUE	20	30	20	15	10	25	19	15	TRUE	3	3	3	9
28	256518881082	SYED HASAN AL JEELANI QUADRI	19	30	19	15	9.5	25	18.5	15	TRUE	20	30	20	15	10	25	19	15	TRUE	4	3	2	9
29	256518881083	SYED MOHAMMED NASIR	15	30	15	15	7.5	25	16.5	15	TRUE	25	30	25	15	12.5	25	21.5	15	TRUE	3	3	3	9
30	256518881084	SYED NASER UDDIN	19	30	19	15	9.5	25	18.5	15	TRUE	25	30	25	15	12.5	25	21.5	15	TRUE	4	2	3	9
31	256518881085	SYEDA AFREEN FATIMA	22	30	22	15	11	25	20	15	TRUE	25	30	25	15	12.5	25	21.5	15	TRUE	4	2	3	9
32	256518881086	TAHURA FIRDAUS KHAN	14	30	14	15	7	25	16	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	3	3	3	9
33	256518881087	TALLOJU TEJASRI	23	30	23	15	11.5	25	20.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	4	2	3	9
34	256518881088	TARIKUL ISLAM	16	30	16	15	8	25	16	15	TRUE	23	30	23	15	11.5	25	19.5	15	TRUE	4	2	2	8
35	256518881089	TEJAVATH RAMA KRISHNA	14	30	14	15	7	25	16	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	3	3	3	9
36	256518881091	THOTA AISHWARYA	20	30	20	15	10	25	19	15	TRUE	23	30	23	15	11.5	25	20.5	15	TRUE	3	3	3	9
37	256518881092	TONDUPALLI SAI PRAKASH REDDY	20	30	20	15	10	25	18	15	TRUE	21	30	21	15	10.5	25	18.5	15	TRUE	3	3	2	8
38	256518881093	TOWSIF AHAMED	18	30	18	15	9	25	17	15	TRUE	20	30	20	15	10	25	18	15	TRUE	3	2	3	8

39	2565188881094	VADTHYAVATH SWAPNA	23	30	23	15	11.5	25	20.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	3	3	3	9
40	2565188881095	VEEPURI UMESH KUMAR	22	30	22	15	11	25	20	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	4	2	3	9
41	2565188881096	VIDYA KUMARI	18	30	18	15	9	25	18	15	TRUE	24	30	24	15	12	25	21	15	TRUE	3	3	3	9
42	2565188881097	ABDUL JUNAID	21	30	21	15	10.5	25	13.5	15	TRUE	22	30	22	15	11	25	19	15	TRUE	3	2	3	8
43	2565188881098	SOMARAJU SAHITH	19	30	19	15	9.5	25	13.5	15	TRUE	21	30	21	15	10.5	25	19.5	15	TRUE	4	3	2	9
44	2565188881099	ALLA DEEPAK SUNDER	18	30	18	15	9	25	17	15	TRUE	21	30	21	15	10.5	25	18.5	15	TRUE	3	2	3	8
45	2565188881100	ABU HASAN	18	30	18	15	9	25	18	15	TRUE	15	30	15	15	7.5	25	16.5	15	TRUE	3	3	3	9
											44									45				

97.77778

100

co	co assessed	level	Internal 0.25 (I)	External	ec. Level	ex.0.75 (E)	Final level I+E	
co1	97.77	3	0.75	68	2	1.5	2.25	
co2	97.77	3	0.75	68	2	1.5	2.25	
CO3	97.77	3	0.75	68	2	1.5	2.25	
co4	100	3	0.75	68	2	1.5	2.25	
co5	100	3	0.75	68	2	1.5	2.25	
co6	100	3	0.75	68	2	1.5	2.25	

St. Pauls College of Pharmacy

B.Pharmacy IV Sem- Sec-A (2019-20)

CONSOLIDATED MARKS STATEMENT

SUB: Medicinal chemistry

S. No.	H.T.No.	Student Name	Theory									Practical							
							Contineous Mode									Contineous Mode			
			I Mid (30M)	II Mid (30M)	AVG. (30M)	AVG./2 (15M)	Attend. (=M)	Acad. Actvt. (3M)	Student teacher inter. (3M)	Total (10M)	Grand Total (25M)	I Mid (40M)	II Mid (40M)	AVG. (40M)	AVG./4 (10M)	Attend. (2M)	Record & viva (3M)	Total (5M)	Grand Total (15M)
1	256517881003	KARNATAKA NAVEEN	13	24	18.5	9.25	3	2	3	8	17	32	34	33	8.25	2	2	4	12.25
2	256517881008	MALLELA HARI PRASAD	13	23	18	9	3	2	3	8	17	32	34	33	8	2	2	4	12.25
3	256517881027	ALIGE NITHYANANDAM	14	21	17.5	8.75	3	2	3	8	17	32	33	32.5	8	2	2	4	12.125
4	256517881040	KOSGI BAL REDDY	14	23	18.5	9.25	3	2	3	8	17	32	34	33	8.3	1	2	3	11.25
5	256518881001	A PAVAN KUMAR GOUD	22	25	23.5	11.75	4	3	3	10	22	32	35	33.5	8.4	2	3	5	13.375
6	256518881002	ABDULLAH QUDUS	23	19	21	10.5	3	3	2	9	20	35	34	34.5	8.6	2	2	4	12.625
7	256518881003	ABDUR RAKIB	AB 17	Ab 18	AB 18	AB 9	2	3	3	8	8 17	AB 36	AB 32	AB 34	AB 8	1	2	3	5 11
8	256518881004	ADIPELLI SAIMEGHANA	18	11	14.5	7.25	4	3	3	10	17	34	36	35	9	2	3	5	13.75
9	256518881006	AHMED BIN HUSSAIN DAYANI	15	20	17.5	8.75	3	3	3	9	18	33	33	33	8	2	3	5	13.25
10	256518881007	AJMAL HOSSAIN	17	20	18.5	9.25	3	3	3	9	18	34	34	34	8.5	2	2	4	12.5
11	256518881008	ANAM FATIMA	23	19	21	10.5	4	3	3	10	21	34	35	34.5	8.6	2	3	5	13.625
12	256518881009	ANDUGULA RAJESHWARI	17	23	20	10	3	3	3	9	19	32	36	34	8.5	1	2	3	11.5
13	256518881010	ARIF SK	19	Ab	19	9.5	3	2	3	8	18	32	AB	32	8	2	3	5	13
14	256518881011	AVURAKONDA MANOJ	13	Ab	13	6.5	4	3	2	9	16	AB 32	AB 24	AB 33	AB 8.3	2 1	2	4 3	11
15	256518881012	AYESHA KOUKAB	23	18	20.5	10.25	3	2	3	8	18	33	34	33.5	8.4	2	3	5	13.375
16	256518881013	AYESHA OSMAN	19	10	14.5	7.25	4	3	2	9	16	34	35	34.5	8.6	2	3	5	13.625
17	256518881015	BALGURI SAVITHA SAGAR	21	20	20.5	10.25	3	3	3	9	19	32	36	34	8.5	2	2	4	12.5
18	256518881016	BALUGURI ANALIKA	18	24	21	10.5	4	3	3	10	21	36	35	35.5	8.9	2	3	5	13.875
19	256518881017	BUSHRA SULTANA	23	19	21	10.5	4	3	3	10	21	35	35	35	9	2	3	5	13.75
20	256518881018	DEPALLY TEJASWI	22	25	23.5	11.75	4	2	3	9	21	33	36	34.5	8.6	2	3	5	13.625
21	256518881019	E SRIHARI	21	22	21.5	10.75	4	3	2	9	20	32	34	33	8.25	2	3	5	13.25
22	256518881020	GANGOLU MANASA	18	22	20	10	4	3	3	10	20	35	33	34	8.5	2	2	4	12.5
23	256518881021	GILKATHULA ANAND	19	22	20.5	10.25	3	3	3	9	19	36	37	36.5	9.1	2	3	5	14.125
24	256518881022	GUDEM VAISHNAVI	18	19	18.5	9.25	4	3	3	10	19	32	35	33.5	8.4	2	3	5	13.375
25	256518881023	GUNDOJU NIHARIKA	19	23	21	10.5	4	3	3	10	21	34	36	35	8.75	2	3	5	13.75
26	256518881024	GURLA NIKHITHA	19	20	19.5	9.75	4	2	3	9	19	34	35	34.5	8.6	2	3	5	13.625
27	256518881025	GURRAM MANASA	22	25	23.5	11.75	3	3	3	9	21	35	36	35.5	8.9	2	2	4	12.875
28	256518881027	HENA RUSKAR	18	22	20	10	4	2	3	9	19	32	34	33	8.25	2	3	5	13.25
29	256518881028	IZAZ AHAMMED	17	20	18.5	9.25	4	3	2	9	18	28 AB	30 AB	AB 29	AB 7	2 1.5	3 1	5 2.5	5 10
30	256518881029	JALAPALA SHAMBAVI	18	22	20	10	3	3	3	9	19	31	36	33.5	8.4	2	3	5	13.375
31	256518881030	JINNIKUNTLA SANTHOSHA	23	23	23	11.5	4	3	2	9	20	32	35	33.5	8.4	2	2	4	12.375
32	256518881031	JUVERIYA SULTANA	22	25	23.5	11.75	4	2	3	9	21	36	36	36	9	2	3	5	14
33	256518881032	KATTUKURI NIKITHA	24	24	24	12	4	3	3	10	22	34	37	35.5	8.9	2	3	5	13.875
34	256518881033	KETHAVATH JHANSI	18	22	20	10	4	3	3	10	20	33	34	33.5	8.4	1	3	4	12.375
35	256518881034	KOTTE SAIVEENA	17	25	21	10.5	3	3	3	9	20	34	37	35.5	8.9	2	2	4	12.875
36	256518881035	KUCHIPUDI DIVYA	19	22	20.5	10.25	4	3	2	9	19	33	34	33.5	8.4	2	3	5	13.375
37	256518881037	KUTUBUDDIN SK	19	24	21.5	10.75	3	3	3	9	20	34	36	35	8.75	2	2	4	12.75
38	256518881038	LAGALA NIVIDHA	20	22	21	10.5	4	3	3	10	21	33	37	35	8.75	2	2	4	12.75
39	256518881039	LAVADIYA BALAJI	19	22	20.5	10.25	4	3	3	10	20	32	36	34	8.5	2	2	4	12.5
40	256518881040	MALLOJU SHIVA KUMAR	20	25	22.5	11.25	4	3	3	10	21	32	34	33	8.25	2	3	5	13.25
41	256518881041	MANDALA SWATHI	20	23	21.5	10.75	4	2	3	9	20	33	38	35.5	8.9	2	3	5	13.875
42	256518881043	MANIRUL HOQUE	16	20	18	9	3	3	3	9	18	31	37	34	8.5	2	3	5	13.5
43	256518881045	MASUDUR RAHAMAN	18	20	19	9.5	3	3	3	9	19	31	AB	31	7.75	2	3	5	12.75
44	256518881047	MD AMIR HAMZA	19	22	20.5	10.25	3	3	3	9	19	33	34	33.5	8.4	2	2	4	12.375
45	256518881048	MD FIZE	16	11	13.5	6.75	3	3	2	8	15	32	35	33.5	8.4	2	3	5	13.375
46	256518881050	MD TASLIM	16	19	17.5	8.75	4	3	3	10	19	AB 30	AB 28	AB 29	AB 7	1 1.5	3 1	5 2.5	10

St. Pauls College of Pharmacy

B.Pharmacy IV Sem- Sec-B (2019-20)

CONSOLIDATED MARKS STATEMENT

SUB: Medicinal chemistry-I

S. No.	H.T.No.	Student Name	Theory									Practical							
			I Mid (30M)	II Mid (30M)	AVG. (30M)	AVG./2 (15M)	Continuous Mode				Grand Total (25M)	I Mid (40M)	II Mid (40M)	AVG. (40M)	AVG./4 (10M)	Continuous Mode			Grand Total (15M)
							Attend. (4M)	Acad. Actvt. (3M)	Student teacher inter. (3M)	Total (10M)						Attend. (2M)	Record & viva (3M)	Total (5M)	
1	256518881051	MD NASER	17	24	20.5	10.25	4	2	3	9	19.25	35	35	35	8.75	2	3	5	13.75
2	256518881052	MOHD ABDULLAH	16	25	20.5	10.25	3	3	3	9	19.25	36	36	36	9	2	2	4	13
3	256518881053	MOHAMMED MUSHRAF	19	25	22	11	4	2	3	9	20	37	37	37	9.25	2	3	5	14.25
4	256518881055	MOHD SHOIAB AFROSE	22	25	23.5	11.75	3	3	2	8	19.75	35	35	35	8.75	2	2	4	12.75
5	256518881056	MUAZZAM ALI	10	21	15.5	7.75	3	3	3	9	16.75	36	36	36	9	1	3	4	13
6	256518881057	MUBEENA SULTANA	19	23	21	10.5	4	3	2	9	19.5	37	37	37	9.25	2	2	4	13.25
7	256518881058	N SATHWIKA	23	21	22	11	4	2	3	9	20	35	35	35	8.75	1	3	4	12.75
8	256518881059	NAIK AZHARUDDIN	19	22	20.5	10.25	4	2	3	9	19.25	36	36	36	9	2	2	4	13
9	256518881060	NAKKILLA VENKATA BHARGAVI	25	22	23.5	11.75	4	3	3	10	21.75	37	37	37	9.25	2	3	5	14.25
10	256518881062	NENAVATH SARASWATHI	23	21	22	11	3	3	3	9	20	35	35	35	8.75	1	2	3	11.75
11	256518881063	OMER BIN KHALID BIN NASIR	19	25	22	11	3	3	2	8	19	36	36	36	9	2	3	5	14
12	256518881064	P LAVAN KUMAR	20	21	20.5	10.25	4	2	3	9	19.25	37	37	37	9.25	1	2	3	12.25
13	256518881065	PASUKULA SANJANA	23	21	22	11	3	3	3	9	20	35	35	35	8.75	2	3	5	13.75
14	256518881066	POGAKU RAVI TEJA	21	21	21	10.5	4	2	2	8	18.5	36	36	36	9	1	2	3	12
15	256518881067	POLISHETTY BALA ROHINI	22	21	21.5	10.75	3	3	3	9	19.75	37	37	37	9.25	2	3	5	14.25
16	256518881068	POLISHETTY RAHUL	22	21	21.5	10.75	4	2	3	9	19.75	35	35	35	8.75	2	2	4	12.75
17	256518881069	PURRE REECHA	23	21	22	11	3	3	3	9	20	36	36	36	9	2	3	5	14
18	256518881070	RAHUL MOLLA	22	22	22	11	4	3	3	10	21	37	37	37	9.25	2	3	5	14.25
19	256518881071	ROBIUL ISLAM	14	22	18	9	4	2	2	8	17	35	35	35	8.75	2	3	5	13.75
20	256518881073	SAMREEN FATIMA	25	22	23.5	11.75	3	3	2	8	19.75	36	36	36	9	1	3	4	13
21	256518881074	SANA BEGUM	22	23	22.5	11.25	4	2	3	9	20.25	37	37	37	9.25	2	3	5	14.25
22	256518881075	SARA FATIMA	18	23	20.5	10.25	3	2	3	8	18.25	35	35	35	8.75	2	3	5	13.75
23	256518881077	SHANIGARAM ANUSHA	22	21	21.5	10.75	3	3	3	9	19.75	36	36	36	9	1	2	3	12
24	256518881078	SHANIGARAM MAHESH	20	21	20.5	10.25	3	2	3	8	18.25	37	37	37	9.25	2	2	4	13.25
25	256518881079	SIRIPURAM SOUMYA	12	23	17.5	8.75	4	3	2	9	17.75	35	35	35	8.75	2	3	5	13.75
26	256518881080	SOHA MASI	21	23	22	11	3	3	3	9	20	36	36	36	9	1	2	3	12
27	256518881081	SYED FARHAN	16	20	18	9	3	3	3	9	18	37	37	37	9.25	2	3	5	14.25
28	256518881082	SYED HASAN AL JEELANI QUADRI	19	20	19.5	9.75	4	3	2	9	18.75	AB	AB	AB	AB	2	3	5	5
29	256518881083	SYED MOHAMMED NASIR	15	25	20	10	3	3	3	9	19	36	36	36	9	1	2	3	12
30	256518881084	SYED NASER UDDIN	19	25	22	11	4	2	3	9	20	37	37	37	9.25	2	2	4	13.25
31	256518881085	SYEDA AFREEN FATIMA	22	25	23.5	11.75	4	2	3	9	20.75	35	35	35	8.75	1	3	4	12.75
32	256518881086	TAHURA FIRDAUS KHAN	14	23	18.5	9.25	3	3	3	9	18.25	36	36	36	9	2	3	5	14
33	256518881087	TALLOJU TEJASRI	23	21	22	11	4	2	3	9	20	37	37	37	9.25	2	2	4	13.25
34	256518881088	TARIKUL ISLAM	16	23	19.5	9.75	4	2	2	8	17.75	35	35	35	8.75	2	3	5	13.75
35	256518881089	TEJAVATH RAMA KRISHNA	14	23	18.5	9.25	3	3	3	9	18.25	36	36	36	9	2	3	5	14
36	256518881091	THOTA AISHWARYA	20	23	21.5	10.75	3	3	3	9	19.75	37	37	37	9.25	2	2	4	13.25
37	256518881092	TONDUPALLI SAI PRAKASH REDDY	20	21	20.5	10.25	3	3	2	8	18.25	35	35	35	8.75	2	3	5	13.75
38	256518881093	TOWSIF AHAMED	18	20	19	9.5	3	2	3	8	17.5	36	36	36	9	2	2	4	13
39	256518881094	VADTHYAVATH SWAPNA	23	21	22	11	3	3	3	9	20	37	37	37	9.25	2	2	4	13.25
40	256518881095	VEEPURI UMESH KUMAR	22	21	21.5	10.75	4	2	3	9	19.75	35	35	35	8.75	2	3	5	13.75
41	256518881096	VIDYA KUMARI	18	24	21	10.5	3	3	3	9	19.5	36	36	36	9	1	2	3	12
42	256518881097	ABDUL JUNAID	21	22	21.5	10.75	3	2	3	8	18.75	37	37	37	9.25	2	3	5	14.25
43	256518881098	SOMARAJU SAHITH	19	21	20	10	4	3	2	9	19	35	35	35	8.75	2	2	4	12.75
44	256518881099	ALLA DEEPAK SUNDER	18	21	19.5	9.75	3	2	3	8	17.75	36	36	36	9	2	3	5	14
45	256518881100	ABU HASAN	18	15	16.5	8.25	3	3	3	9	17.25	37	37	37	9.25	2	2	4	14.25

Code No. 6056/PCI

FACULTY OF PHARMACY

B. Pharmacy IV-Semester (PCI) (Suppl.) Examination, January 2020

Subject: Medicinal Chemistry - I

Time: 3 Hours **Max. Marks: 75**

Note: Answer All questions from PART-A, any TWO questions from PART-B and any SEVEN questions from PART-C.

PART-A (10 x 2=20 Marks)

1 Define ionization. Give the equation to calculate % drug ionized.
2 *o*-Salicylicacid is more active than *p*-hydroxybenzoicacid. Why?
3 Write a note on adrenergic receptors and their distribution.
4 Write the structure and uses of naphazoline and tolazoline.
5 Write the synthesis of carbachol.
6 Write the structure and MOA of pralidoxime chloride.
7 Define sedatives and hypnotics with examples.
8 Give the structure and uses of haloperidol.
9 Define narcotic antagonists with examples.
10 Give the synthesis ofibuprofen.

PART-B (2 x 10 = 20 Marks)

11 (a) Explain in detail about conjugation reactions. (6M)
(b) Explain the factors affecting drug metabolism. (4M)

12 (a) Write a note on SAR of morphine analogues. (5M)
(b) Classify cholinolytic agents with examples. (5M)

13 (a) Wrlte SAR and MOA of barbiturates. (5M)
(b) Write the synthesis and uses of phenytoin and chlorpromazine hydrochloride. (5M)

PART- C (7 x 5=35 Marks)

14 Explain the significance and determination methods of partition coefficient.

15 Wrlte SAR of sympathomlmetlcagents.

16 Write synthesis of salbutamol and phenylephrine.

17 Write MOA of cholinesteraseinhibitors.

18 Write the biosynthesis and catabolism of acetylcholine.

19 Classify adrenergic antagonists with examples.

20 Classify antipsychotics with examples.

21 Write synthesis and uses of halothane and ketamine hydrochloride.

22 Write structure and uses of following drugs

(A) aspirin (B) mefenamic acid (C) ibuprofen (D)acetaminophen (E) diclofenac.

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Code No. 13191/PCI

FACULTY OF PHARMACY

B. Pharmacy IV Semester (PCI) Main Examination, July 2019

Subject: Medicinal Chemistry – I

Time: 3 Hours **Max. Marks: 75**

Note: Answer ALL questions from PART-A, any TWO questions from PART-Band any SEVEN questions from PART-C.

PART – A (10 x 2 = 20 Marks)

1. Define hydrogen bonding and its effect on biological activity of drugs.
2. Mention phase –II reactions?
3. Write any two applications of cholinesterase inhibitors with example of drugs .
4. Write the synthesis of propranolol.
5. Define adrenergic antagonists with examples.
6. Explain cholinergic blocking action with an example of drug.
7. Give the synthesis of phenytoin.
8. Define antipsychotics with examples.
9. Give the structures for fentanyl citrate and methadone hydrochloride.
10. Give the structures for aspirin and antipyrine.

PART – B (2 x 10 = 20 Marks)

11. Define and give the significance of the following physicochemical parameters on biological activity (3+3+4)
    (a) Ionization (b) Chelation (c) Protein binding.

12. (a) Write in detail about MOA of Parasympathomimetics. (5)
    (b) Classify antiinflammatory agents with examples. (5)

13. (a) Write a note on SAR of benzodiazepines. (5)
    (b) Write the synthesis and uses of barbital and carbamazepine. (5)

PART – C (7 x 5 = 35 Marks)

14. Explain the significance of bioisosterism in relation to biological activity with examples.
15. Write a note on biosynthesis and catabolism of Catecholamines.
16. Write in detail about SAR of beta blockers.
17. Classify sympathomimetics with examples.
18. Write the synthesis of dicyclomine hydrochloride and ipratropium bromide.
19. Write SAR of Parasympathomimetics.
20. Classify anticonvulsants with examples.
21. Give an account on general anesthetics.
22. Discuss in detail about SAR of morphine analogues.

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Code No. 6249/CBCS

FACULTY OF PHARMACY

B. Pharmacy V Semester (CBCS) (Backlog) Examination, October 2020

Subject: Medicinal Chemistry-I

Time: 2 Hours **Max. Marks: 70**

Note: Answer any four questions. **(4x17½=70 Marks)**

1. What are the physic chemical factors that effects the drug action and explain how partition coefficient effect the drug action with examples?

2. Explain the concept of Bioisosterism and explain Drug metabolism in detail.

3. Classify adrenergic blocking agents and write mechanism of action, SAR and synthesis of
   a) proazocin
   b) Atenelol

4. Write a note on neuromuscular blocking agents and explain mechanism of action and synthesis of Mecamylamine HCl.

5. Classify cardiovascular agents and write the synthesis of
   a) Captopril b) Clonidine
   c) Nifedipine d) Clofibrate

6. a. Classify Antihyperipedemics? Explain SAR of HMG CoA reeducates inhibitors.
   b. Classify Antihypertensives! Explain SAR of centrally acting drugs.

7. Classify Diueretics? Write the SAR and synthesis of
   a. Acetazolamide
   b. Furosemide

8. a. Write a brief account on thyroid and antithyroid drugs.
   b. Write a short note on Immunosuppressant and immunostimulants.

9. Classify Anti histaminics? Write the synthesis and SAR of
   a) Diphenhydramine
   b) Chlorpheniramine

10. a. Write a brief note on coagulants and anticoagulants.
    b. Write a brief account on Proton pump inhibitors and anti histaminics.

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St. PAULS COLLEGE OF PHARMACY
Turkayamjal, Hyderabad 501510.
Result analysis B.PHARM IV SEM PCI
(2018 - 2022 BATCH)
Exam held in NOV/DEC 2020.
Results declared on 28/01/2021
OVERALL ANALYSIS

Batch	Appeared	Passed (Class)			PASSED	Failed	DETAINED	Pass %
		II	I	Distinction				
92	91	--	--	----	38	53	---	41.75%

No. of Students with Backlogs:

Sl.No	No. of Backlogs	No. of Students
1	1 Subject Fails	18
2	2 Subject Fails	16
3	3 Subject Fails	11
4	4 Subject Fails	05
5	5 Subject Fails	03

Name of Subject	No. of Students Appeared	No. of Students Passed	No. of Students Failed	Pass Percentage (%)
MEDICINAL CHEMISTRY - I	91	60	31	65.9 %
PHARMACEUTICAL ORGANIC CHEMISTRY - III	91	71	20	78.0 %
PHARMACOGNOSY AND PHYTOCHEMISTRY - I	91	62	29	68.1 %
PHARMACOLOGY - I	91	61	30	67.0 %
PHYSICAL PHARMACEUTICS - II	91	82	9	90.1 %

EXAM BRANCH

PRINCIPAL
Principal
St. Paul's College of Pharmacy
Turkayamjal, R R District.