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SYNTHESIS AND MODE OF ACTION OF TRICYCLIC ANTIDEPRESSANTS

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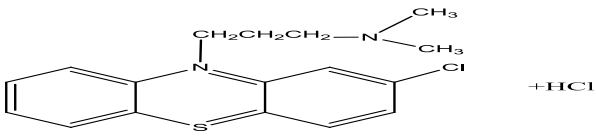
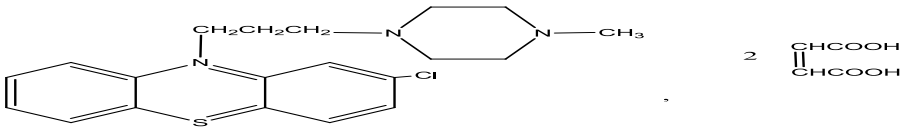
ABSTRACT
Depression is now common problem in human being. Antidepressive drugs are used to elevate the mood in depressive illness. All antidepressants affect, monoaminergic transmission in the brain mainly two types are antidepressant drugs which are tricycle Antidepressants and Monoamine oxidase inhibitors. They inhibits monoamine uptake and interact with a variety of receptors such as muscarine, histamine H_1 and α-adrenergic,5-hydroxytryptamine 1 and 2 and occasionally with dopamine D_2.TCA_S and related drugs inhibit active uptake of biogenic amines. Tricyclic Antidepressantsareimipramine, Amitriptyline, Doxepin, Dothepin Clomipramieandadrenalineinhibitorsas Desipramine, Notriptyline, amoxapine.

KEYWORDS: Depression Tricyclic Antidepressantsareimipramine, Amitriptyline, amoxapine.

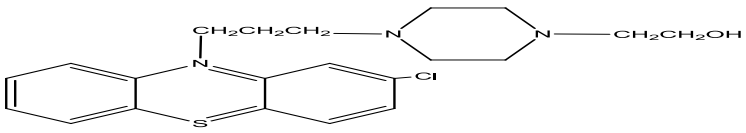
INTRODUCTION
Depression is now common problem in human being; it can be appeared at any time. Depressed person may be suffered from symptom characteristics. As sadness, hopelessness, Despair, inferiority, suicidal-preoccupation, Episodic-Frequency, insomnia; Somatic symptoms are constipation, weight loss and Headache; psychotic symptoms are Delusions, Hallucinations and Depersonalization. Antidepressive drugs are used to elevate the mood in depressive illness. All antidepressants affect, monoaminergic transmission in the brain mainly two types are antidepressant drugs which are tricycle Antidepressants and Monoamine oxidase inhibitors. Tricyclic Antidepressantsareimipramine, Amitriptyline, Doxepin, Dothepin Clomipramieandadrenalineinhibitorsas Desipramine, Notriptyline, amoxapine. Tricyclic Antidepressants (TCA_Sinhibitsmonoamine uptake and interact with variety of receptors such as muscarcarine, histamine H_1,α-,5hydroxytryptamine1 and 2 and occasionally with dopamine D_2.



Chloropromazine Hydrochloride



Prochloroperazine Maleate



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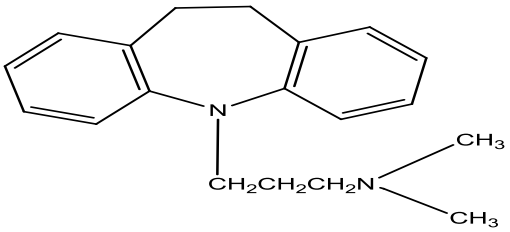

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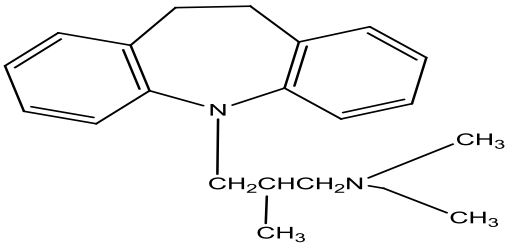
Imparamine Hydrochloride



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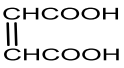
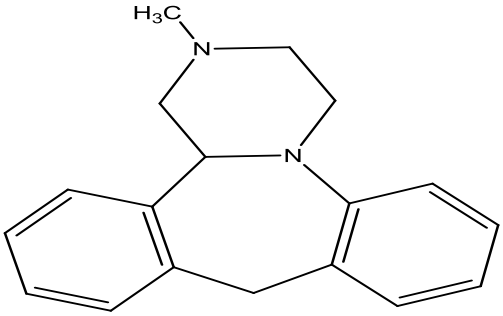


TriImparamine Maleate



HCl

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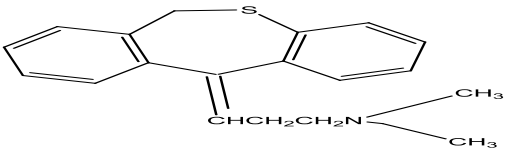
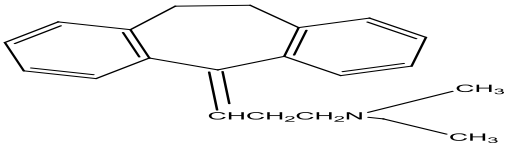
Mianserin Hydrochloride



Dothiepin Hydrochloride



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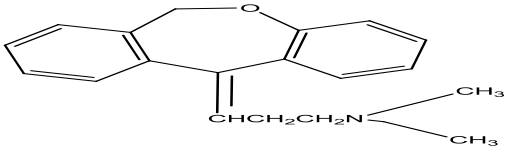
AmitriptylineHydrochloride



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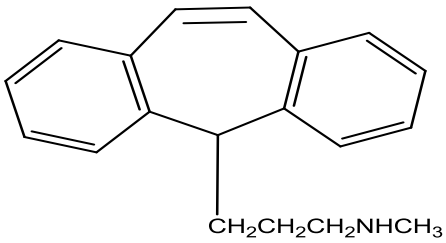
Doxepin Hydrochloride



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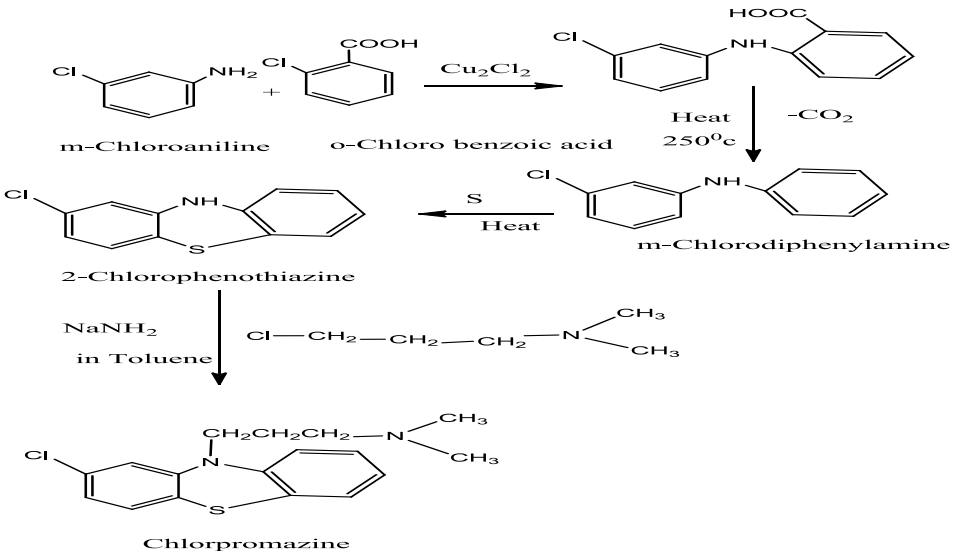
Protriptyline Hydrochloride

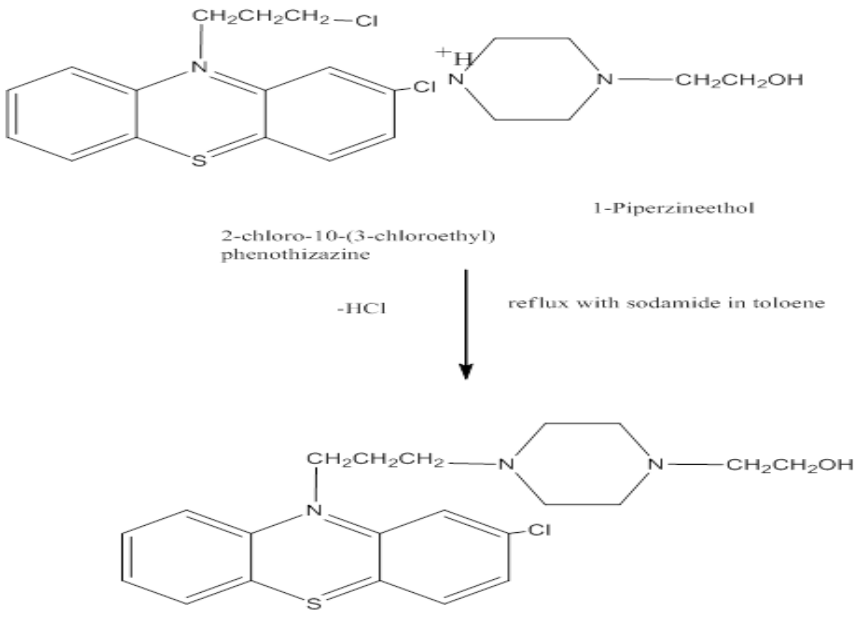
Synthesis

1. **Chlorpromazine**



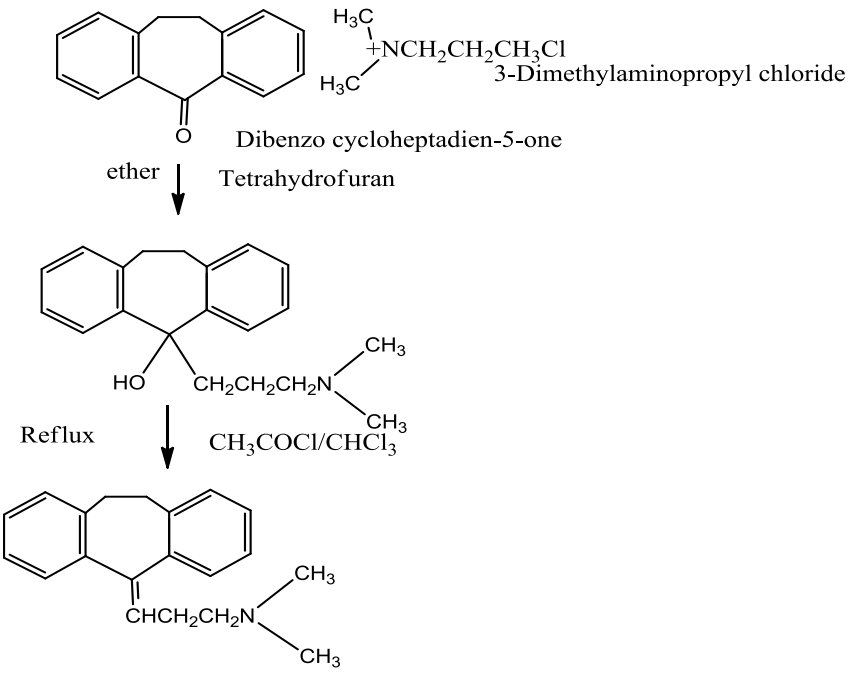
2.

Prephenazine



Prephenazine

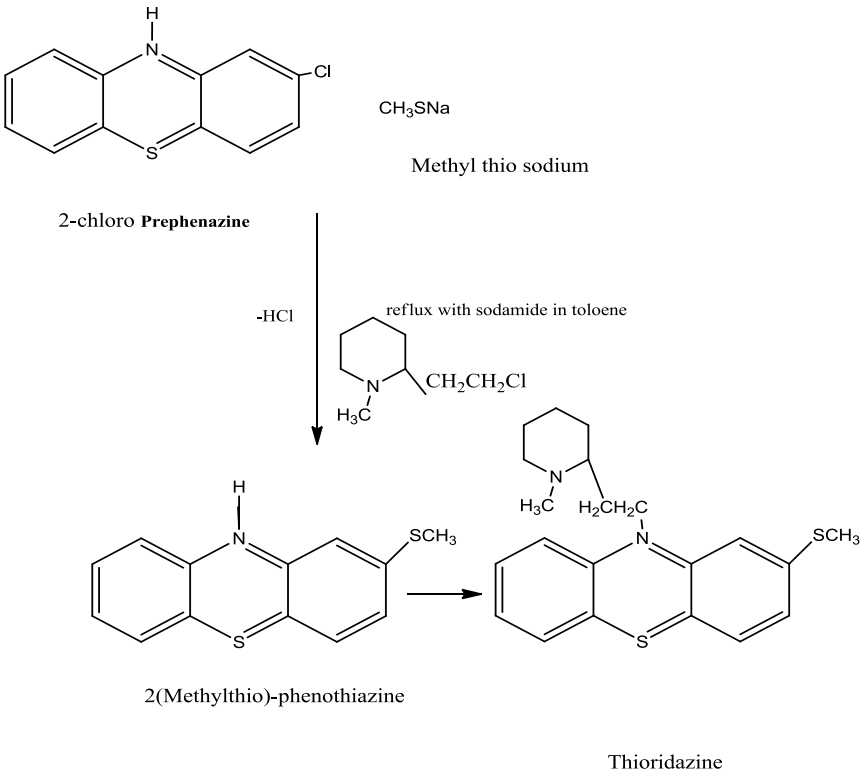
Amitriptyline



Amitriptyline

3.

Thioridazine

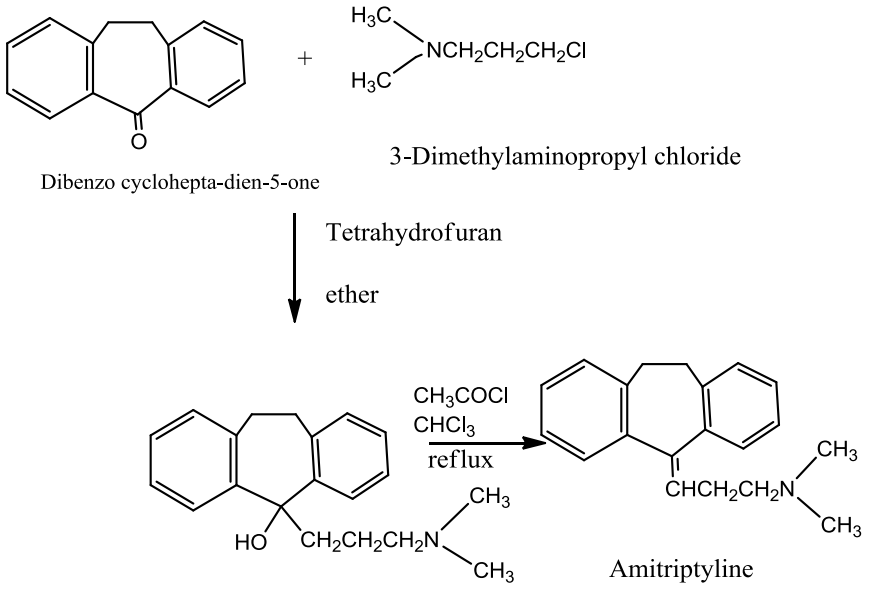


2(Methylthio)-phenothiazine

Thioridazine

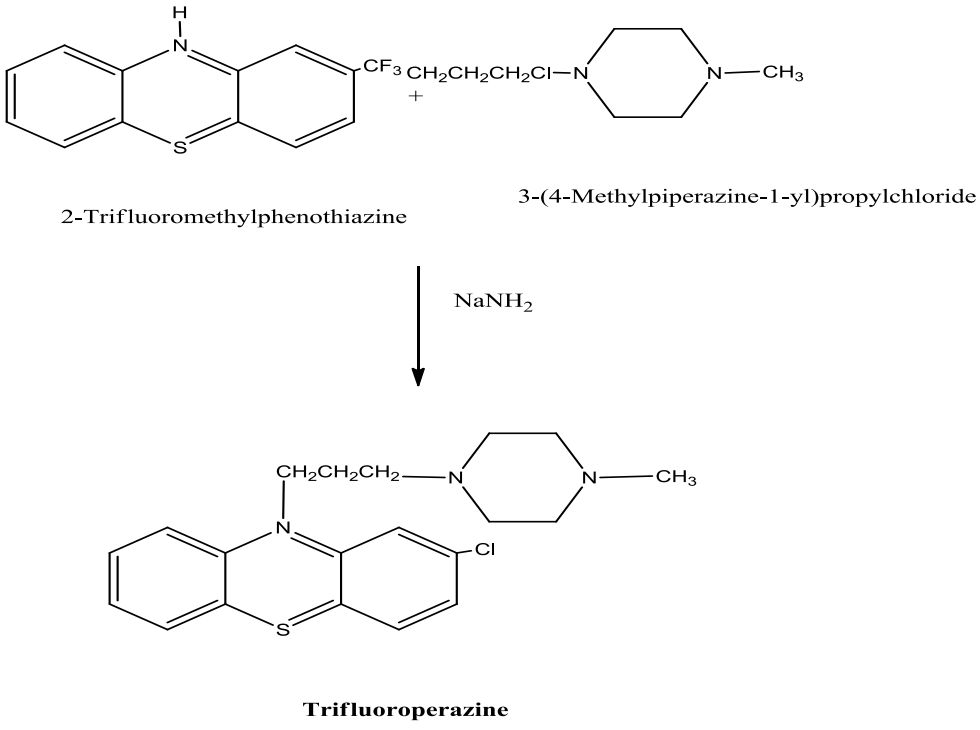
4.

Amitriptyline

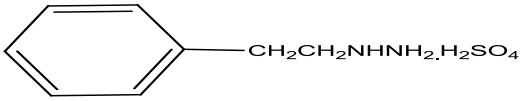


5.

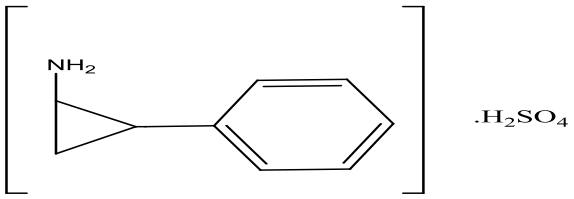
Trifluoroperazine



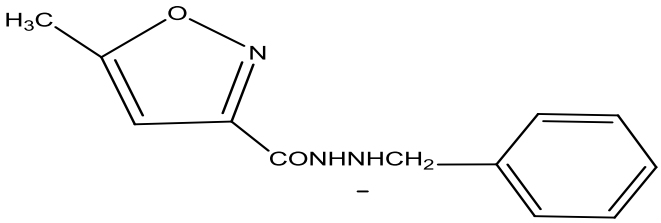
Monoamine Oxidase Inhibitors(MAO)



Phenelzine Sulphate



Tranylcypromine Sulphate



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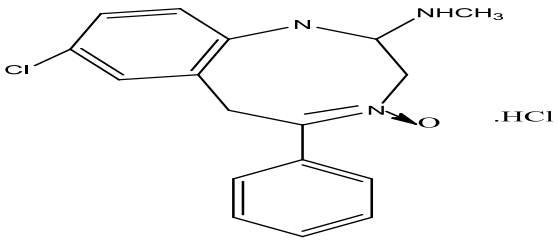
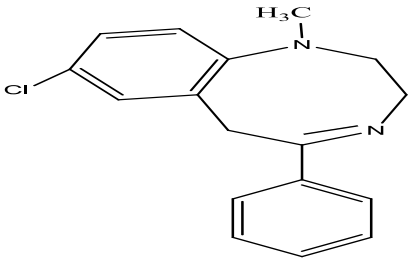
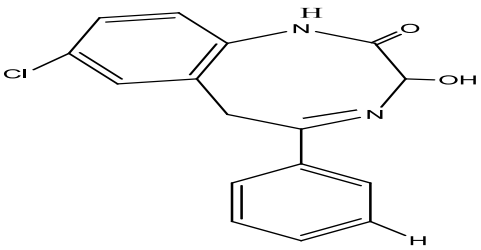


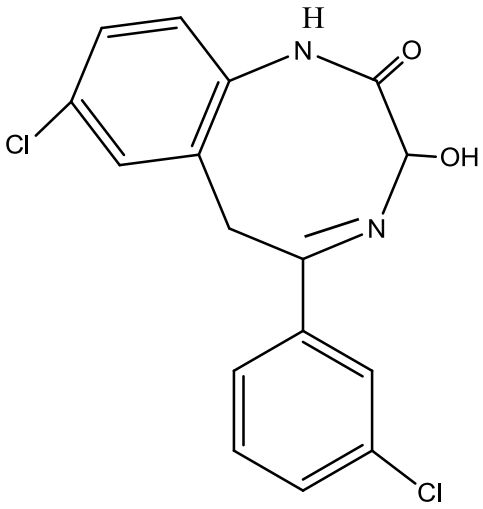
Chlordiazepoxide Hydrochloride



Diazepam



Oxazepam



Lorazepam

Mode of Action

Tricyclic Antidepressants(TCA_S): They inhibits monoamine uptake and interact with a variety of receptors such as muscarine, histamine H_1andα-adrenergic, 5-hydroxytryptamine 1 and 2 and occasionally with dopamine D_2.TCA_S and related drugs inhibit active uptake of biogenic amines.

In depressed patients little acute effects are produced by TCA_S, except sedation. After giving these drugs continuously 2to 3 weak the mood of patients is gradually elevated and becomes more communicated and start taking interest in self and surrounding. This, TCA_S are not euphorients but only antidepressants, in not proper sleep these drugs are more applicable and this phase is suppressed awakening during night are reduced. The more sedative drugs are suitable for depressed patients showing anxiety and agitation. The less sedative drugs are better for withdrawn and retarded patients. The TCA_S lower seizure threshold and convulsion in over dose. Clomipramine; maprotiline and bupropion have the highest seizure precipitating potential. Amitriptyline and imipramine depress respiration in overdose only TCA_S and related drugs inhibit active uptake of biogenic amines. TCA_S and related drugs inhibit active uptake of biogenic amines Noradrenalin and 5-HT (5-hdroxy Tryptamine) into their respective neurons and thus potentiate them. They differ in their selectivity and potency for different amines. Most of the compounds do not inhibit DA (Dopamine) uptake, except bupropion, Amphetamine and cocaine which are strong inhibitors of Dopamine uptake they are not antidepressants but can play important role in Central nervous system stimulation. However, it has been found that TCA_S indirectly facilitate dopaminergic transmission in forebrain that may play role in mood elevation. Inhibition of DA uptake correlates with stimulant action but it is not involved basically in antidepressant action and inhibition of NA (Noradrenaline) and5-HT (5-hdroxy Tryptamine).

Several findings indicate that uptake blocked is not directly responsible for antidepressants action, uptake blockade occurs quickly but antidepressant action appears after few weak now considering mainserin is one of the antidepressant but does not show blocking action. Initially the presynapticα_2 and 5-HT_1autoreceptors are activated by the increased amount of NA/HT in the synaptic cleft resulting in the decreased firing of locus coeruleus (noradrenergic) and raphe (serotonergic) neurons. On long term administration antidepressants desensitise presynaptic α_2,5-HT_{1A},5-HT_{1D} auto receptors and induce other adaptive changes in the number and sensitivity of pre and post synaptic NAand/or5-HTreceptors as well as in amine turnover of brain, finally it is found the enhancement noradrenergic and serotonergic transmission. Thus, uptake blockade appears to initiate a series of time dependent changes that culminate in antidepressant effect. Most tricyclic antidepressant is more potent anticholinergic which show adverse effect as dry mouth, blurring of vision, constipation and urinary hesitancy. They show effect on cardiovascular function and may be dangerous in over dose. They potentiate exogenous and endogenous NA by blocking uptake, having weakα_1 adrenergic blocking action for example amitriptyline, doxepin, trimpramine show slight H_1 antihistaminic action.

MAO is a mitochondrial enzyme which plays a role in oxidative deamination of biogenic amines as adrenalin, norepinephrine, dopamine and 5-hydroxy tryptamine. MAO-A deaminates norepinephrine and 5-hydroxy tryptamine and are inhibited by clorgynline and moclobemide. MAO-B deaminates phenyl ethylamine

and is inhibited byseligiline. Dopamine can be deaminated by both the is enzymes.

CONCLUSION

TCA_S potentiate CNS depressants; including alcohol and antihistaminic which also abolish the antihypertensive action of guanethidine and clonidine by preventing their transport into adrenergic neurons. They potentiate directly actin sympathomimetic amines and inhibits the action of indirect sympathomimetics. They have good oral absorption which are metabolise in liver, the major route for imipramine and amitriptyline is demethylation whereby active metabolites-desipramine and nortriptyline respect are formed. Mechanism of action of anti-depressants drugs is based on activities of the tricyclic antidepressants agents.

It is suggested that the antidepressants drugs increase the availability of biogenic amines at their post synaptic receptor site in brain and reverse the depression. Imprtant drugs which are tricycle are imipramine, Amitriptyline, Doxepin, clomipramine and Trimipramine.

REFERENCES

1. Jenner, P.; Marsden, C.D.,(1985) Drugsin Central Nervous System Disorders, New York, D.C. Horwell Ed.
2. Sepinwal, J. andcook, L.(1978), Handbookof Psychopharmacology, vol.13, New York, plenum.
3. Braestrup,c.; Nielsen.(1983) Handbookof Psychopharmacology, 17.
4. Williams, R.L. and Kareacan, I.(1976) Pharmacology of sleep Newyork, John Wily
5. Sternback, L.H., et, al; (1968) Drugsaffectingthecentralnervoussystem,vol.2, A. Burger, Newyork, Marcel Dekker.
6. Gordon.(1967); Psychopharmacological Agents; New York, Academic press.
7. Chatwal G.R.(2012) Medicinal chemistry(2nd.ed) - Himalayan Publishing HouseIndia(chapter-7).
8. Gupta A.(2015) Medicinal chemistry (1st.ed) - Pragati Prakshan Merutt (chapter-3).
9. Ochai. E.-I (1987) General Principles of Biochemistry of the Elements. Plenum, New York
10. Gray, H.B. (1986.) Chem. soc. Rev. 1986.
11. chmidt. R.F, Fundamental of Neurophysiological 1978, Springer Verlog, 2nd ed.