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EVALUATION OF ANTICONVULSANT ACTIVITY OF L-DEPRENYL IN ALBINO WISTAR RATS

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Abstract

This study was to investigate the anticonvulsant action of L-deprenyl and its possible mechanism of action in Albino wistar rats. Maximum Electroshock Seizure (MES) and Pentylene tetrazole induced seizures were used as experimental models to study the anticonvulsant effect in albino wistar rats L- Deprenyl has shown an Alarming effect in most of the experimental models. In the present study, L-Deprenyl has shown dose dependent protection against MES convulsions. L-Deprenyl did not provide any significant protection against PTZ induced convulsions but in combination with imipramine the anticonvulsant effect was appreciable. Thus in conclusion it can be said that L-Deprenyl can be used as an effective anticonvulsant drug apart from D-Deprenyl available in market.

Keywords **:** L-Deprenyl, Anticonvulsant, Electroshock, Wistar, albino

Introduction

The term convulsion is defined as an abrupt alteration in cortical electrical activity, manifested clinically by a change in consciousness or by motor, sensory or behavioral symptoms (Plim, 1985). Convulsion may occur as a result of epilepsy, toxic manifestations of the use of central nervous system stimulants and are observed in Eclampsia, Uremia, Hypoglycemia, Hyperthermia and Pyridoxine deficiency. A number of neurotransmitters are involved in convulsive disorders mainly Gamma amino butyric acid (GABA), Hydroxytrytamine, nor - epinephrine, Acetylcholine and Glutamate. Chemicals like pentylenetetrazole, Biculline, Picrotoxin, and Strychnine are known to induce convulsions in rats and mice (Wolfag *et al*., 1995). Most of these agents induce convulsions by antagonising or inhibiting the actions of GABA.L- Deprenyl a drug which has shown anti-parkinson's activity in its previous studies is used as a monotherapy in early parkinsons disease. It is an irreversible inhibitor of MAO type B which has been used in the therapy of Parkinsons disease since 1986 (Wofgan *et al*., 1995). Apart from MAO type B inhibition, it also exerts several effects on Dopamine and Noradrenaline systems. L-Deprenyl improves the performance of patients with Alzheimer's disease. It has been suggested that a drug combining cognition enhancing and antiepileptic activity would be of beneficial in the treatment of epileptic patients. Preliminary experiments suggest that L Deprenyl exerts effects on convulsions in rat kindling model (Holland *et al*., 1965). L – Deprenyl is more potent than D - Deprenyl in anticonvulsant activity. This promoted us to study the anticonvulsant effect of L-Deprenyl in other convulsive models. L Deprenyl may be used prophylactically for slowing down convulsions. Furthermore, based on animal data (Stevens J.R *et al* ., 1969). it has been proposed that the normal age dependent rate of decline of the striatal dopaminergic system, thereby decreasing the risk of age - related neurological diseases. The present study is to investigate -the anticonvulsant action of L-deprenyl and its possible mechanism of action.

Materials and Methods

Albino rats of either sex weighing 150-250 gm., L-Deprenyl: 5gm tablet, Imipramine: 75mg tablets. The animals were kept in the animal house of Shadan College of Pharmacy.

Chemically induced convulsions

Animals were placed in individual boxes. Pentylene tetrazole was administered and convulsions were noted for 10 sec as per the procedure devised by (Vasu *et al*., 1975).

Electroshock- Induced convulsions

In this model electric shock was used to induce convulsions in rats. The rats were given electro shocks of alternating current of 150 milli amp for 0.2 Sec (Corcora *et al*., 1980).

Results

Effect of L-Deprenyl On MES Convulsions

L-Deprenyl (5mg/kg) provided no protection against convulsions after 30 minutes, but shows 50% protection after 60 minutes, and at (10mg/kg) dose levels, it shows 0% protection after 30 minutes but 66.6% protection after 60 minutes. L-Deprenyl (10mg/kg) decreases the mean latency of test group (2.96) compared to the control group (4.32). It is insignificant L-Deprenyl decreases the mean duration of tonic convulsions of test group (3.71) compared to mean duration of tonic convulsions of control group (6.98), which is significant but is insignificant ($p > 0.05$). L - Deprenyl (10mg/kg) provided significant protection as compared to control against MES induced convulsions ($p < 0.05$), Fisher exact test.

Effect of Imipramine on MES Convulsions:

Imipramine (10mg/kg) provided 33.3% and 50% of protection after 30 mins and 60 mins, and at (15mg/kg) dose levels it provided 50% and 100% of protection after 30 and 60 mins. Imipramine (15mg/kg) decreases the mean latency of test group (1.31) compared to the mean latency of control group (2.48) which is insignificant statistically ("p" value >

0.05). It also decreases the mean duration of convulsions of test group (3.36) compared to mean duration of control group (10.15), which is significant statistically ("p" < 0.05). Imipramine (15 mg/kg) provided significant protection as compared to control against MES induced convulsions (p < 0.05, Fisher exact test).

Effect of L-Deprenyl with Imipramine on MES induced convulsions:

L-Deprenyl (5 mg/kg) provided no protection after 30 minutes and 50% of protection after 60 minutes, but in combination with Imipramine (10 mg/kg) it shows 90% protection after 60 minutes and 50% protection after 30 minutes. Imipramine (10 mg/kg) provides 33.3% and 0% protection after 30 minutes and 60 minutes.)

Effects of L-Deprenyl in Pentylenetetrazole induced convulsions

L-Deprenyl (5 mg and 10 mg) provided no protection against PTZ induced convulsions. The mean latency (66.33) ofL-Deprenyl (5mg/kg) treated group is decreased compared to the mean latency of control group (71.66)" which was insignificant. Though the mean latency (100) of L-Deprenyl (10 mg/kg) treated group is increased compared to control group it is statistically insignificant "P" > 0.05. L-Deprenyl (5 mg and 10 mg) showed insignificance in mean duration compared to mean duration of control groups "P" > 0.05.

Table 1: Anticonvulsant effect of Deprenyl in Maximal electroshock convulsions in rats

S. No	Drug	Experimental Method	Dose mg/Kg	Time 30mins	60mins
1	L-Deprenyl	MES	5	66.6%	100%
2	L-Deprenyl	MES	10	100%	100%
3	L-Deprenyl	MES	15	0%	50%
4	Imipramine	MES	5	0%	66.6%
5	Imipramine	MES	10	33%	50%
6	Imipramine	MES	15	50%	100%
7	Imipramine & L-Deprenyl	MET	10, 5	90%	100%

Table 2: Protective effect of Deprenyl in pentylene tetrazole induced convulsions

S. No	Dose mg/kg	Latency (sec)	Duration (sec)	Drug
1	5	71.66 ±14.37	42.50±6.89	Pentylene Tetrazole (PTZ)
2	5	66.33±11.84	43.66±9.89	PTZ+L-Deprenyl
3	10	100±72.60	34.16±16.85	PTZ+L-Deprenyl
4	5ml/kg	0.48±00.87	10.15±00.99	Saline
5	15	04.32±00.77	06.98±0.98	PTZ+L-Deprenyl

Discussion

There are many chemical substances available which are known to induce convulsions by different mechanisms, like increase in 5-HT activity, increase in nor-epinephrine activity and inhibition of GABA activity (Hublin *et al*., 1994)There are two types of drugs, which stimulates the central nervous system. Drugs which are nonspecific CNS stimulants, when they are administered produce a powerful CNS excitation. e.g. Pentylenetetrazole (PTZ) Bhadhuri *et al*., 1980). Drugs whose main effects are not CNS excitation but when given in higher does they may produce CNS excitation. Convulsions can also be produced by Electric shock in two ways that is MET and MES. It is use as cognition enhancing agent in Alzheimer's disease (Gloor *et al*., 1974) In the present study, L-Deprenyl has shown dose dependent protection against MET and MES convulsions and the protection against the MET was significantly higher than against MES Our results support the reported hypothesis of L-Deprenyl that it preferentially inhibits focal seizure activity as compared to seizure spread. In the present study, L-Deprenyl has not provided any significant protection like, Latency, duration and frequency of convulsions against PTZ induced convulsions and provided a significant protection against picrotoxin induced convulsions regarding frequency and duration of convulsions.

Looking at the reports on anticonvulsant action of L-Deprenyl (5mg, 10mg &15mg) against PTZ (60 mg/kg) it is assumed that L-Deprenyl does not act by stimulating GABA minigic neurotransmissions or by stimulating increased synthesis of GABA. But taking into consideration, the mean duration and Frequency of convulsions which are significant in L-Deprenyl treated groups (10mg &15mg) as compared to the control picrotoxin (2mg / kg) treated group. We can assume that L-Deprenyl may also act partially by enhancing presynaptic inhibitor action of GABA.

Our study suggests that L-Deprenyl is effective against MET and MES convulsions and ineffective against chemically induced convulsions. The anticonvulsant mechanism might be due to its inhibition of re-uptake of monoamines, MAO- B inhibition, neuroprotective effect and probably due to an increased cholinergic activity. However, further studies are necessary to know the mechanism in its anticonvulsant action.

Conclusion

In the conclusion the anticonvulsant activity of L-Deprenyl in different samples has shown much a tremendous effect. There are many anticonvulsant drugs present in the market. Thus the present investigation shows that L-Deprenyl has shown much anticonvulsant effect than D-Depenyl already available in market.

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