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NEUROPROTECTIVE EFFECT OF ETORICOXIB AGAINST THE HALOPERIDOL INDUCED PARKINSONS DISEASE IN MICE.

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Abstract:
Parkinson's disease (PD), is characterized by slow and progressive degeneration of dopaminergic neurons in substantia nigra per compacta of the central nervous system (CNS). Neuroinflammatory mechanisms might contribute to the cascade of events leading to neuronal degeneration. In the present study we examined the protective effect of etoricoxib, against the haloperidol induced Parkinson's diseased in mice. In the present study mice treated with the Haloperidol (1mg/kg/day) by IP route. where orally dose with etoricoxib and L-dopa/carbidopa for 14 days was given. Motor assessment test like catalepsy, wire hanging test, & open field test was measure on 7th day and 14th day of dosing. Also the assessment of memory was carried out by using the water maze test and passive avoidance test. After performing this test we found that haloperidol induced group reduced the motor function on catalepsy test, open field test, and wire hanging test as compare to control, standard and test drug group. Cataleptic behaviour of all animal were evaluated at 7th & 14th day at the time interval 5,60, 120,180 min. for the cut of time 180sec post hoc analysis is performed by Bonferroni test show that Ip administration of haloperidol produced significant catatonia($P<0.001$). In passive avoidance ($P<0.001$)test etoricoxib treated group significantly decreased the escape latency after 7th day as compare to control standard and test drug treated group. And in water maze test($P<0.001$)etoricoxib treated group significantly increase the escape latency time as compare to control standard and test drug. the present work provide an evidence that etoricoxib increase behavioural performances by mediating neuroprotection against haloperidol induced PD via preventing dopaminergic neuronal cell death

Keywords: Neuroinflammation. Parkinson's disease. Neurodegenerations, NSAIDs,

I. Introduction:

Parkinson's disease (PD) is a chronic neurodegenerative disease that is generally differentiated by the reduction in motor functions caused on by the dysfunction of the dopaminergic nigrostriatal pathway. The predominant motor symptoms, such as tremor at rest, bradykinesia, rigidity, and postural instability, are specifically caused by the death of dopaminergic neurons that project from the substantia nigra pars compacta to the caudate-putamen in the striatum[1].

This symptoms are influenced by non-motor abnormalities, such as olfactory dysfunction, constipation, and sleep difficulties, as well as predisposing factors like depression[2]. The presence of LBs, which are defined as intracellular cytoplasmic aggregates made of proteins, lipids, and other components, is the other key histological characteristic of PD. Additionally, major characteristics of LBs have been linked to chronic neurodegenerative disorders, such as PD[3]. Non-steroidal anti-inflammatory agents (NSAIDs) have anti-inflammatory, analgesic, and antipyretic effects. They also block the enzyme cyclooxygenase (COX), which is involved in the production of prostaglandin precursors from arachidonic acid. NSAIDs also inhibit activation of neutrophils, which induce inflammation by releasing products COX-1 and COX-2, increasing prostaglandins, which may aggravate inflammation[4]. According to research, neurodegenerative diseases and neuroinflammation is responsible for the activation of glial cells, primarily microglia and astrocytes, and the generation of important inflammatory mediators as well as damaging free radicals are characteristics of inflammation in the brain. According to several studies Anti-inflammatory drug use may reduce the risk of developing Parkinson's disease (PD) in people, The goal of this study is to identify the used of NSAIDs in PD[5].The main objective of this study is to evaluate the neuroprotective activity of non-steroidal anti-inflammatory drug in haloperidol induced Parkinson disease.

II. Materials & Methods :

2.1 Drug &Chemicals –

Etoricoxib drug was obtain as a gift sample from Admiron life sciences private limited. Levodopa and carbidopa tablet ip (1:4) was purchased from sun pharma laboratories limited. Haloperidol injection IP (serenace) manufacture by RPG life science Ltd was used to induced parkinsonism.

2.2 Experimental animal:

Experiment would perform in accordance with the committee for the purpose and supervision of experimental animals (CPCSEA) guidelines after the approval of the experimental protocol by the Institutional Animal Ethical committee (IAEC). • The mice of either sex would be used for the study. The animal would be housed 5 per cage at temperature (25+1'C) with 50±5% of relative humidity under 12 h day and night cycle fed standard rodent chow and water. Animal were acclimatized to laboratory conditions before the experiment were started.

2.3 Induction of parkinsonism: Parkinsonism induced in mice by using the haloperidol as an anti-psychotic drug. The most frequent dose of haloperidol used was 1.0 mg/kg, standard bar test was used to assess the catalepsy, Haloperidol, an antipsychotic that acts as a D2 receptor antagonist, used mainly to control the agitation and aggressiveness presented during the acute phase of schizophrenia, can cause extrapyramidal side effects, such as akinesia and rigidity of movements. intraperitoneal administration of haloperidol can induce the catalepsy. Haloperidol-induced catalepsy results from the blockage of D2 dopaminergic receptors in the nigrostriatal pathway and is often used as an animal model for the study of motor impairments observed in parkinsonian disorders. Experiments with this model are generally confirmed in an animal model of neurodegeneration. Neurodegeneration models can be instructive in modelling the different stages of dopamine loss during the progression of PD, from the initial stage, in which compensatory mechanisms still allow the maintenance of adequate motor function, until the late stages of the disease, in which the loss of dopamine is so drastic that the motor symptoms appear.

2.4 Experimental Protocol :

Total 30 animals are divided into five group. all the mice were trained before starting the dosing protocol for the assessment of passive avoidance test, Morris water maze test, & wire hanging test. Group 1- control group received saline solution only(10ml/kg) Group 2- Negative control received haloperidol only (1mg/kg Ip) Group 3- oral suspension of L-dopa/ carbidopa(20mg/kg p.o)+ Received haloperidol (1mg/kg ip) Group 4- - Oral suspension of etoricoxib (6mg/kg p.o)+ Received haloperidol (1mg/kg ip) Group 5- Oral suspension of etoricoxib (10 mg/kg p.o)+ Received haloperidol (1mg/kg ip) Haloperidol injection are given intraperitoneal route 30min before the standard & test drug Behavioural study & spacial memory studies were carried out at the day 7th, 14th , days of study.

2.5 Behavioural assessment:

A) Catalepsy test:

The catalepsy was assessed as the time during which the mouse maintained an imposed position with both forelimbs extended and rested on a 4 cm high wooden bar (1 cm in diameter). The endpoint of catalepsy was considered to occur when both forepaws were removed from the bar or if the animal moved its head in an exploratory manner. A cut-off time of 180s was applied. Between the 2 determinations, the animals were returned to their home cages. All the observations were made in a quiet room at 23-25°C. As for the scoring method, if the animal maintained the imposed posture for at least 20s it was considered to be cataleptic and the time was recorded in seconds.[6]

B) Locomotor activity:

Actophotometer

An actophotometer was used to assess the horizontal & vertical spontaneous moments of the animal. Set up comprises of an electronic unit and infrared beam . chamber complete with two sets of sensor arrays for horizontal & vertical activity the animal was placed into metal chamber for 5 min. the moment makes inside the chamber interrupt one or more infrared beams. The beam interruptions are counted and recorded by the electric devices. The test was performed on the, 7th, 14 th, day of dosing. For testing, each mouse was individually placed in an activity cage for 5 min after 30, 60, and 120 min of dosing, and total locomotor activity was recorded .[7]

C) Grip strength test:

Wire hanging test Gripping strength of animal was assessed by using wire hanging test. Apparatus consisted of stainless-steel bar with two platform, mice were briefly trained before the test session. The animal were placed separated on stainless steel bar the wire stretch between two 30cm pole and hang 70cm above the foam cushion and allowed the gripping the bar to observed the grip strength and muscular tone. The length & time the mice was able to hold the bar till it fell was recorded at 7th & 14th days of treatment with cut off time of 300 sec.[8]

2.6 Assessment of memory

A) Water maze test:

Water maze test is used to assess the spatial learning behaviour of the rodents. The water maze apparatus consisted of a rectangular transparent Plexiglas tank(60 ×30 cm) that was filled with tap water. Water was maintained at room temperature. The depth of water maze is 12cm. the water was made opaque in order to hide the platform from the animal via dissolving starch in it. A platform (15x13cms) made of Plexiglas was fixed; the water level was kept 2cm above the surface of platform. Initially the rats were trained before the test session. During the training period each animal was individually placed in the water facing the wall of the tank. Rats were allowed to locate and climb onto the submerged platform and allowed to stay on the platform for 10 seconds. Cut-off time for the test is 2 minutes. If the animal failed to find the platform within the allowed time it was guided gently onto the platform. Memory of the animals was evaluated by recording retention latency. The time that animal takes to reach the platform is taken as “retention latency”. Retention latency (in seconds) was noted during the test session after 1 hour (short term memory) 24 hours (long term memory) after the training of animals. All the mice of control, haloperidol, standard and test groups were tested for their short-term memory after 7th 14th days of treatment .[9]

B) **Passive avoidance test:**

Effect of antipsychotic drug on memory function was evaluated using a passive avoidance test. The step through passive avoidance task may be regarded as a measure long-term memory acquisition. the pre-treated animals were placed in an illuminated box (101315 cm) connected with larger (25 20 15 cm) dark compartment equipped with an electric grid floor. In this test, entry into the dark compartment was punished by an electric footstock (0.6mA for 2sec). the mice that did not enter the dark compartment within 60 sec were excluded from the experiment. On the following day (24h later), the same animal without any treatment were placed in the illuminated box and those avoided the dark compartment for longer than 180 sec were regarded as remembering the task. Retention was evaluated as median in sec with 25 & 75 percentiles required to entered the dark compartment.[10]

Data analysis : All the data is presented as mean ± SEM (n=6) results. Statistical evaluation was perform using Graph Pad prism software version 9.1 by using one way ANOVA followed by Bonferroni multiple comparison test was used for post hoc analysis.

Results :

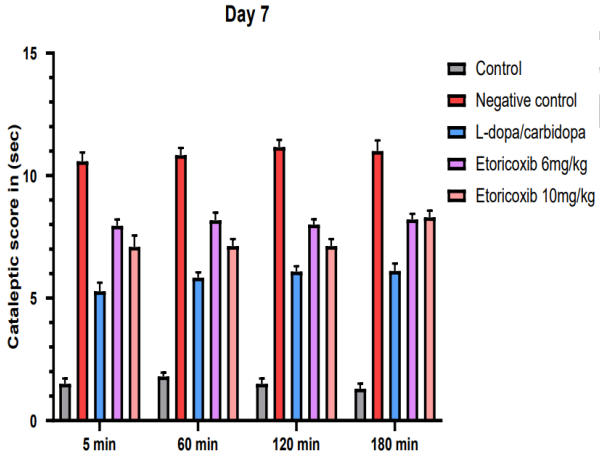
Table No 1 : Effects of etoricoxib on catalepsy in haloperidol induced Parkinson disease.

7th day Cataleptic Score(Cut off time 3min)

Test	Groups					
Catalepsy	Time In Min	Control(10ml/kg p.o)	Negative Control(Haloperidol 1mg/kg i.p)	Standard Drug(L-dopa/carbidopa)	Etoricoxib(6mg /Kg P.O)	Etoricoxib(10 mg/Kg P.O)
	5	1.5±0.22	10.58±0.37	5.28±0.35	7.95±0.26	7.02±0.47
	60	1.8±0.16	10.83±0.30	5.83±0.22***	7.95±0.26	7.12±0.29***
	120	1.5±0.22	11.16±0.30	6.08±0.22***	7.12±0.22***	7.12±0.29***
	180	1.3±0.21	11±0.44	6.11±0.30***	8.21±0.23***	8.3±0.27***

Values are expressed as a mean ±SEM n=6

***P< 0.001 when compare with control & negative control



Graph No 1: Effect of etoricoxib on catalepsy bar test in haloperidol induced parkinson's disease

Cataleptic behavior of all animal was evaluated at 7th day at the time interval 5,60, 120,180 min. for the cut of time 180sec post hoc analysis is performed by Bonferroni test show that ip administration of haloperidol produced significant catatonia, when compare with control group, after the 7th 5 min of dosing 10.58±0.37 (P<0.001) which then significantly increase by time. The cataleptic score increases to 10.83±0.30(P<0.001) on 60 minute 11.16±0.30 (P<0.001) on 120min, & finally to 11±0.44 (P<0.001) while etoricoxib treated group show significant reduction in cataleptic score as indicated by significant(P<0.001) reduction in time spend on the bar test. After (7.02±0.47) on 5min, (7.12±0.29) 60 min, on (7.12±0.29), 120 min, 180 (8.3±0.27) when compare with negative control group. This results show that cataleptic latency time was reduced

Table No.2 :Effects of etoricoxib on catalepsy in haloperidol induced Parkinson disease14th day

Test	Time (min)	Groups				
		Control saline solution (10 ml/kg p.o)	Negative control Haloperidol(1mg/kg i.p)	Standard Levodopa/Carbidopa (20mg/kg p.o)	Etoricoxib6 mg/kg p.o	Etoricoxib 10mg/ kg p.o
Catalepsy Test	5	1.28±0.09	11.13±0.48	5.9±0.19	9.3±0.21	9.25±0.21
	60	1.3 ±0.16	12.13±0.32	6.08±0.25***	9.45±0.19*	9.3±21***
	120	1.41±0.20	14±0.39	6.25±0.24***	9.5±0.22***	9.45±0.21***
	180	1.5±0.21	15.36±0.26	6.3±0.21***	9.6±0.19***	9.5±0.61***

Values are expressed as a Mean±SEM n=6.***P <0.001 When compare with control & negative control.

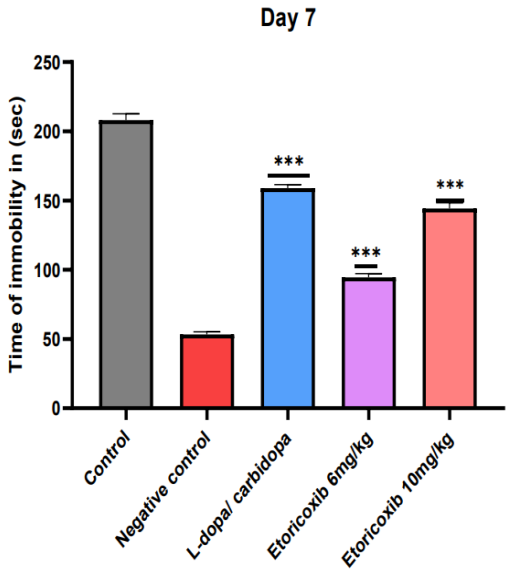
Cataleptic behavior of all animal was evaluated at 14th day at the time interval 5,60, 120,180 min. post hoc analysis is performed by Bonferroni test show that Ip administration of haloperidolproduced significant catatonia, when compare with control group , after the 7th day after the 5 min of dosing 11.13±0.48 (P<0.001) which then significantly increase by time. The cataleptic score increased to 12.13±0.32 (P<0.001) on 60 min, to 14±0.39 (P<0.001) on 120 min, & finally to 15.36±0.26 (P< 0.001) while etoricoxib treated group show significant reduction in cataleptic score as indicated by significant(P<0.001) reduction in time spend on the bar test. After the 5 min (9.25±0.21), 60 min (9.3±21),120 min (9.45±0.21), 180 (9.5±0.61) when compare with negative control group. This result show that cataleptic latency time was reduced by diclofenactreated group. At the day 7th and it was significantly decrease (P<0.001) at different time intervalwhen compare with negative control group.

Table No.3. Effects of Etoricoxib on Locomotor activity by using Actophotometer in haloperidol induced Parkinson's disease.

Group no	Groups	7th day No of count / 5min	14th day No of count / 5min
1	Control (10 ml/kg p.o)	115.75±27.83	235±1.34
2	Negative ControlHaloperidol (1mg/kg i.p)	53.33±0.76	31.66±1.72
3	Standard drug Levodopa/Carbidopa (20mg/kg p.o)	159±1.0***	90.33±1.64***
4	Etoricoxib (6mg/kg p.o)	94.3±1.11***	72.5±0.42***
5	Etoricoxib (10 mg/kg p.o)	144.33±1.66***	80.83±1.66***

Values are expressed as a mean ±SEM n=6

**P< 0.001 when compare with control negative control



Graph No 3: Effect of Etoricoxib on locomotor activity in haloperidol induced parkinson's disease

In the present study observed that i,p administration of haloperidol shows significant deterioratedmotor neuron in actophotometer after the day 7th ,and 14th Animal treated with haloperidol (1mg/kg ip,) alone for 14 days show the significantly decrease the locomotor activity (P<0.001),The locomotor activity decreases on 7th day, 53.33±0.76 (P<0.001),decrease on 14th day31.66±1.72(P<0.001) when compare with the control group ,

Animal treated with the low dose of etoricoxib(6mg/kg)along with haloperidol(1mg/kg ip)for 14days show significant increase(P<0.001) increase on 7th day, 94.3±1.11 (P<0.001) increase on 14th day 72.5±0.42 (P< 0.001),locomotor activity when compare with the negative control group.Animal treated with high dose (10mg/kg) show significant (P<0.001) increase on 7th day 144.33±1.66(P<0.001), increase on 14th day 80.83±1.66(P<0.001) when compare with negativecontrol group.

Table no.4 Effect of Etoricoxib on wire hanging test in haloperidol induced Parkinson disease

Group no	Doses	7th day	14 th day
1	Control (10 ml/kg p.o)	213.33±1.2	225±0.80
2	Negative Control Haloperidol (1mg/kg i.p)	64.66±1.4	6.16±0.15
3	Standard drug Levodopa/Carbidopa (20mg/kg p.o)	76.16±1.64***	92.5±1.6***
4	Etoricoxib 6mg	71.33±1.4***	108.33±1.72***
5	Etoricoxib 10 mg	72.16±0.91***	96.33±1.5***

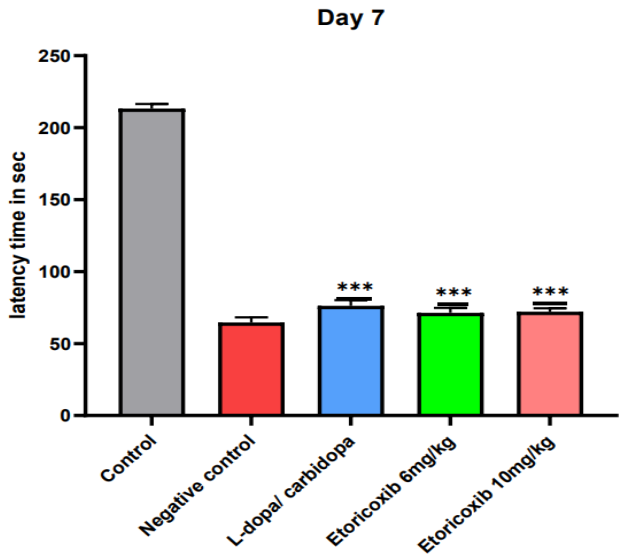
Values are expressed as a mean ±SEM n=6

***P< 0.001 when compare with control negative control

Wire hanging test is used to determine grip strength & muscular tone in mice. In present study i,p administration of haloperidol significantly reduced the muscular tone & hanging time 5 min in mice 64.66±1.4,(P<0.001) as compare to control group after the 7th day & further gradually decrease on 14th day of treatment 6.16±0.15 (P<0.001) as compare to control & test drug.

Animal treated with low dose of etoricoxib (6mg/kg) along with haloperidol for 14 days show significantly, increase the hanging time & muscular tone on 7th day 71.33±1.4 (P<0.001)Increaseon 14th day 108.33±1.72(P< 0.001)

Animal treated with Etoricoxib (10mg/kg) along with haloperidol show significant increase the hanging time & muscular tone on 7th day 72.16±0.91(P<0.001) increase on 14th day 96.33±1.5(P<0.001)



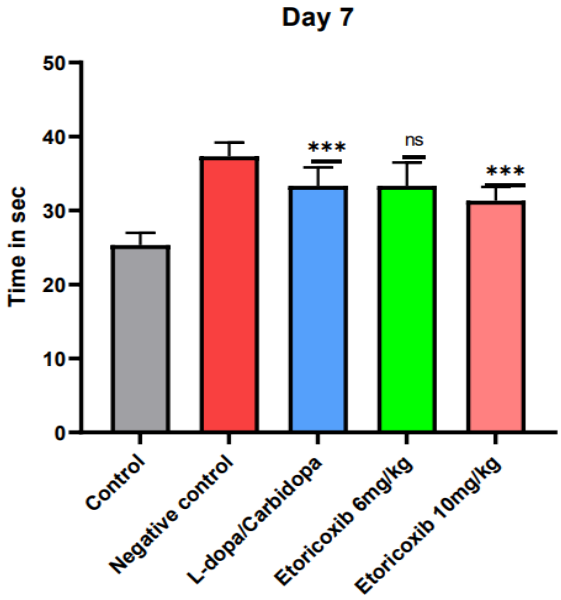
Graph No.5 Effect of Etoricoxib on wire hanging test in haloperidol induced parkinsons disease

Table no.5 Effect of Etoricoxib on Morris water maze test in haloperidol induced Parkinson disease

Group No.	**Doses**	**7th day**	**14th day**
1	Control (10 ml/kg p.o)	25.33±0.66	20.66±0.84
2	Negative Control Haloperidol (1mg/kg i.p)	37.33±0.76	70.5±1.33
3	Standard drug Levodopa/Carbidopa (20mg/kg p.o)	33.33±1.02***	9.05±0.29***
4	Etoricoxib 6mg	31.33±0.17	16.16±0.60***
5	Etoricoxib 10 mg	33.33±1.2***	13.5±0.76***

Values are expressed as a mean ±SEM n=6 (df-4,25)

***P< 0.001 when compare with control negative control



Graph No 7: Effects of etoricoxib on morris water maze test in haloperidol induced parkinson disease

The short-term learning and memory behavior of mice were assessed by water maze activity, inthis activity ,it was observed that haloperidol induced mice shows more time taken to reach the platform, 37.33±0.76 (P<0.001) after 7 day, on 14 th day highly increase the escape latency wasobserved, 70.5±1.33 (P<0.001) as compare to control, standard & test group.

Animal treated with low dose of etoricoxib (6mg/kg) along with haloperidol for 14 days show nonsignificant increase the latency time on 7th day 31.33±0.17(P>0.05) significantly increase on14th day16.16±0.60(P<0.001).

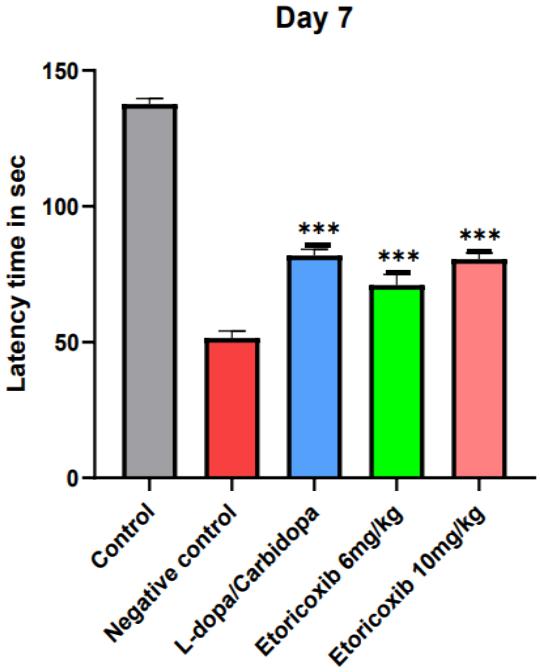
Standard drug33.33±1.02(P<0.001) and test drug(10mg/kg) 33.33±1.2(P<0.01) show significant results on 7-day treatment, whereas ,after 14 day show significant results, with standard drug 9.05±0.29 (P<0.001) , and etoricoxib at dose 10mg/kg 13.5±0.76(P< 0.001).

Table no.6 Effects of Etoricoxib on passive avoidance test in haloperidol induced Parkinson's disease.

Groups	Doses	7 th day	14 th day
1	Control (10 ml/kg p.o)	137.66±0.80	151.16±2.5
2	Negative Control Haloperidol (1mg/kg i.p)	51.5±1.05	26.66±1.02
3	Standard drug Levodopa/Carbidopa (20mg/kg p.o)	81.83±0.94	117.83±1.30***
4	Etoricoxib 6mg	80.5±0.95***	113.83±1.68***
5	Etoricoxib 10 mg	71.0±1.61***	87.33±1.02***

Values are expressed as a mean ±SEM n=6 (df-4,25)

***P< 0.001 when compare with control & negative control



Graph No 9 :Effect of Etoricoxib in passive avoidance test in haloperidol induced parkinson model

Passive avoidance test is fear aggravated test used to evaluate learning & memory in mice in present study i,p administration of haloperidol treated mice decrease the escape latency time 51.5±1.05 (P< 0.001) after 7 days as compare to control. latency time significantly decrease wasfound to be 26.66±1.02(P<0.001) after 14th day of haloperidol treatment.as compare to control group.

Animal treated with low dose of etoricoxib(6mg/kg)along with haloperidol for 14 days show significant increase the latency time on 7th day 80.5±0.95(P<0.001),on 14th day113.83±1.68(P<0.001) when compare with negative control group.

Animal treated with etoricoxib (10mg/kg) along with haloperidol for 14 days show significant increase the latency time on 7th day 71.0±1.61(P<0.001) on 14th day87.33±1.02(P<0.001) when compare with negative control group.

Discussion

In the present study involve evaluation of anti-Parkinson's activity of Etoricoxib on haloperidol induced Parkinson's disease. Etoricoxib could provide the neuroprotective effect in PD by inhibiting the cytokines and prostaglandin upregulation, Etoricoxib is a selective cox-II inhibitor, most commonly used NSAIDs to reduce the pain, inflammation .The main mechanism of action of etoricoxib is to inhibit the cyclo-oxygenase enzyme which is responsible for neuroinflammation in brain .Our findings identified novel pharmacological mechanisms of these drug to exert not only their anti-inflammatory, analgesic, antipyretic activities but also neuroprotective activities against neurodegeneration. In the present study we aimed to explore the neuroprotective role of etoricoxib against haloperidol induced Parkinson's like symptoms. Previous researches explained that NSAIDs, especially etoricoxib, play a major role in inhibiting neuroinflammation due to which it prevent the progression of PD by inhibiting inflammatory cascade. In all treated group haloperidol is a neuroleptic drug used to developed Parkinson disease in an animal model. Haloperidol induced mice model show significant cataleptic score, impaired motor function , & motor coordination after 7th , 14th , day of dosing. treatment with etoricoxib show significantly reduced the cataleptic score and reduced the latency period results are comparable with the negative control group . Oxidative stress occurs as the results of increase free radicals and decrease in anti-oxidant level. That indicate that NSAIDs decrease oxidative stress by inhibiting iNOS and ROS species and increase PPAR. The protective effect of etoricoxib against the haloperidol induced Parkinson models. this suggest that the NSAIDs can be beneficial in Parkinson through inhibition of COX enzyme. Typical neuroleptic agents such as chlorpromazine, haloperidol and reserpine induce a cataleptic state in rodents which is widely used as a model to test the extrapyramidal side effects of antipsychotic agents. Neuroleptic-induced catalepsy has been linked to a blockade of postsynaptic striatal dopamine D1 and D2 receptors. The present study demonstrates the anti-inflammatory & antioxidant effects etoricoxib in haloperidol-induced, cataleptic oxidative stress in mice. The induction of free radicals in mammals by haloperidol is well established. Previous studies have shown that dopamine receptors in the striatum are involved in neuroleptic-induced catalepsy. It has been demonstrated that the cataleptic effects of haloperidol are apparently mediated by dopamine receptors localized postsynaptic on striatal neurons. It is also well established that the administration of haloperidol leads to an increase in the oxidative stress in the brain tissue Weak muscular co-ordination and grip strength were observed in wire hanging test due to haloperidol block the dopamine receptor and monoamine reductase at nerve terminal. etoricoxib treated mice significantly improved their grip strength in wire hanging test. Etoricoxib treated mice significantly improved their motor activities in actophotometer and showed better muscular coordination and grip strength in comparison with L-dopa/carbidopa treated mice after 14 days. The Actophotometer chamber was used to assess the locomotion which marked the mental alertness of animal. Increased number of horizontal and vertical movements across the chamber showed more alertness. In our study, etoricoxib at all dose level cause an increase in movement in chamber. Water maze activities with haloperidol treated rats showed more time taken to locate the platform after 14 days of treatment. This observation is consistent with the recent researchers that explain that haloperidol effectively increases lipid peroxidation, free radical formation as well as decreases glutathione in brain. At 7th day treatment with etoricoxib at low dose did not significantly affect the spatial memory as in Morris water maze test. At 14th day The passive avoidance test showed that latency in haloperidol treated mice was decreased. mice took less time to enter in punishment box (dark box) after 14 days of haloperidol treatment that shows impaired memory and learning behaviour. Treatment with etoricoxib significantly affect their spatial memory & improved learning behaviour, mice took more time to enter in dark box. In experimental models induced free radical formation that produces damage to dopaminergic cells and decreased epinephrine and serotonin concentration which ultimately led to amnesia and learning deficit Although there is still no clear explanation for the intrinsic susceptibility of the dopaminergic neuron of the SNpc, which degenerate in PD, it is know that they are prone and susceptible to oxidative stress. Some hypotheses suggest that primary neurodegeneration in the nigrostriatal pathways leads to increased dopamine turnover and triggers ROS generation. Etoricoxib is a widely used non-steroidal anti-inflammatory drug that rapidly cross blood brain barriers, inhibit neuronal cyclooxygenase enzymes and act as an antioxidant. It also activates nuclear factor peroxisome proliferator-activated receptor (PPARγ) which is neuroprotective in the case of Parkinson's disease. As a result, we suggest that oral usage of low repeated doses of etoricoxib may possibly slow down the progression of disease. Different doses and different uses time are needed to observed the protective effect of this drugs enterally. Further investigation are needed to prove this hypothesis.

Conclusion :

In conclusion Parkinson process led to oxidative stress through inflammatory reactions in mice neuron, etoricoxib prevented the oxidative stress and inflammatory reaction in the CNS in a dosed dependent manner. This is also show that etoricoxib possesses antioxidant activity in addition to anti-inflammatory activity. This property suggest that it can be useful in the prevention of neuro inflammation. since these drug is easily available & clinically proven, with less toxicity, it is worthfull these drug may be used routinely for the effective treatment of parkinsonism.

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