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Integrative Assessment Of Motor Activity And Catalepsy In Albino Rats: Roles Of Citral, Zonisamide, And Monoamine Modulators

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Abstract: *Catalepsy is a neurological finding of prolonged muscular rigidity and immobility, where the individual's limbs remain in an unnatural, fixed posture. The condition results in decreased response to external stimuli and reduced sensitivity to pain. Catalepsy involves a loss of voluntary motion, muscle rigidity, fixed posture, and decreased sensitivity to pain. It is a symptom of a number of conditions including epilepsy, Parkinson's disease, substance use, catatonia, schizophrenia, and as a side effect of some types of medication used to treat schizophrenia. It is a state of immobility and is thought to be associated with the blockade of dopaminergic pathways in the basal ganglia. Monoamine modulators are substances that alter the activity of monoamine neurotransmitters in the brain. These neurotransmitters, including dopamine, serotonin, and norepinephrine, play crucial roles in regulating mood, cognition, and various other brain functions. Monoamine modulators can either enhance or inhibit the effects of these neurotransmitters, leading to changes in neuronal signaling and ultimately affecting behavior and mental state. Catalepsy can be measured by the means of the bar test in experimental animals. In present study an attempt was made to study the Effect of Haloperidol, Zonisamide, Citral, Serotonin analogue antagonist/antagonist, Dopamine analogue antagonist/antagonist on haloperidol induced cataleptic effect in Bar Test*
Keywords: *Citral, Haloperidol, Dopamine analogue antagonist, catalepsy*

INTRODUCTION:

Catalepsy is a neurological finding of prolonged muscular rigidity and immobility, where the individual's limbs remain in an unnatural, fixed posture. The condition results in decreased response to external stimuli and reduced sensitivity to pain. Catalepsy involves a loss of voluntary motion, muscle rigidity, fixed posture, and decreased sensitivity to pain. It is a symptom of a number of conditions including epilepsy, Parkinson's disease, substance use, catatonia, schizophrenia, and as a side effect of some types of medication used to treat schizophrenia. It is a state of immobility and is thought to be associated with the blockade of dopaminergic pathways in the basal ganglia. Catalepsy can be measured by the means of the bar test in experimental animals [1-2].

A somnolent state, characterized by loss of voluntary motion and sensibility, and a peculiar plasticity of the muscles are the cardinal features of catalepsy. The plastic condition of the muscles makes it possible to mold the limbs and body into odd postures which can be retained for long periods. Experiments on cats in which these symptoms have been produced by lesions at the base of the brain in the region of transition between the forebrain and the midbrain have shown that there is no binding relationship between the depth of the somnolence and the ease with which the animals can be made to assume and maintain unusual postures [3-4].

Blocking dopamine receptors with neuroleptic drugs can induce catalepsy, a state of akinesia and rigidity very similar to that seen in Parkinson's disease. Haloperidol is a dopamine D2 receptor antagonist that induces catalepsy when systemically administered to rodents. This cataleptic state provides a simple and useful animal model for investigating the antiparkinsonian potential of drugs. Based on clinical reports of the emotional influence on the motor aspects of Parkinson's disease, currently there exists great interest in knowing whether or not some degree of emotionality underlies catalepsy [5-6].

It is established that the recruitment of dopaminergic mechanisms in the setting up of adaptive responses in threatening conditions will depend on the type of emotional stimuli triggering the coping reaction. For instance, it has been reported that the main characteristics of classical neuroleptic drugs in doses that did not induce catalepsy is the reduction of conditioned avoidance behaviors leaving unchanged unconditioned escape responses in the two-way avoidance test. Thus, studying how dopaminergic

mechanisms are involved in the mediation of distinct kinds of motivational responses could help our understanding on the neural substrates of fear and anxiety [7].

Serotonin plays a complex role in neuroleptic-induced catalepsy, often acting as a modulator of dopamine-mediated movement. Some studies suggest that serotonin can either enhance or antagonize catalepsy depending on the specific receptor subtype and the dose of the antipsychotic. For example, serotonin agonists can sometimes potentiate haloperidol-induced catalepsy, while 5-HT2 receptor antagonists may reduce it. The relationship between serotonin and catalepsy is not straightforward. Serotonin can influence dopamine-mediated motor activity through various pathways, including the modulation of dopamine release and the regulation of dopaminergic neuronal activity [8-9].

Different serotonin receptors (5-HT1A, 5-HT2A, 5-HT3) and their agonists/antagonists can have differing effects on catalepsy. For instance, 5-HT1A receptor agonists can antagonize raclopride-induced catalepsy, while antagonists may enhance it. The effects of serotonin on catalepsy can be dose-dependent, meaning the outcome may vary depending on the concentration of the serotonin agonist or antagonist being tested. Some studies have reported conflicting results regarding the effects of certain serotonin receptor antagonists on haloperidol-induced catalepsy, possibly due to the complexities of the serotonergic system and the interaction with dopamine. Neuroleptic medications, which can block dopamine receptors, can induce catalepsy as a side effect. Serotonin, through its influence on dopamine, can play a role in the expression of this side effect. Studies have also investigated the role of serotonin in hereditary catalepsy, suggesting that genetic variations in serotonin metabolism might contribute to the development of this condition [10-13]. In present study an attempt was made to study the Effect of Haloperidol, Zonisamide, Citral, Serotonin analogue antagonist/antagonist, Dopamine analogue antagonist/antagonist on haloperidol induced cataleptic effect in Bar Test

Subjects: Albino wistar rats, with weights ranging from 200 to 350 g participated in this experiment. The animals were individually housed in 40 × 20 × 24 cm Plexiglas cages with wood shavings as bedding and maintained on a regular 12:12 h light / dark cycle. All behavioural tests were conducted during the light period of the cycle, starting at 9:00 am. All animals had access to food and water without restrictions throughout the duration of the experiment.

Drug and solution:

Haloperidol, Citral, Serotonin analogue antagonist (ritanserin and Glemanserin), Serotonin analogue agonist (Ipsapirone and RU 24969), Dopamine analogue Agonist (Ropinirole and Pramipexole), Dopamine analogue antagonists (Haloperidol and Raclopride) were used in present study were dissolved in sterile saline solution. Various concentrations were made according to doses of respective drug substances.

Model (BAR test)

Catalepsy is a measure of muscular rigidity that can result from several factors including Parkinson's disease, or pharmacological exposure to antipsychotics. Catalepsy bar tests are widely used to measure this rigidity. The test consists of placing the arms of a rodent on a horizontal bar that has been raised off the ground and measuring the time it takes for the subject to remove themselves from this imposed posture. Traditionally, this has been measured by an experimenter with a stopwatch, or with prohibitively expensive commercial apparatus that have issues of their own.

Catalepsy, defined as a reduced ability to initiate movement and a failure to correct abnormal posture, was measured by means of the bar test. To test of catalepsy, animals were positioned so that their hindquarters were on the bench, and their forelimbs rested on a 1 cm diameter horizontal bar, 6–9 cm above the bench. The length of time that animal maintained this position was recorded by stopwatch to a maximum of 180 s (mean of three consecutive trials; interval: 1 min). Animals would determine judge to be cataleptic if they maintained this position for 30 s or more.

Catalepsy animals were placed on an inclined (60°) grid. To establish a reliable baseline, the first 30 s were excluded from the actual rating time. The time the rat remained in the same position was thereafter measured for a maximum of 2.5 min. CAT was scored from 0 ± 5 according to the time (minutes; square root transformation) the animal remained immobile: 0 = 0 ±0.08, 1 = 0.09± 0.35, 2 = 0.36 ±0.80, 3 = 0.81 ± 1.42, 4 = 1.43 ± 2.24, 5 is more than or equal to 2.25, i.e. if the rat remained immobile for more than or equal to 2.25 min, a score of 5 was recorded. The drug injected was haloperidol, administered subcutaneously in the nape of the neck at a dose of 0.5 mg/kg. A saline solution was used as a vehicle. All experimental procedures were initiated 20 min after the drug was injected.

RESULTS

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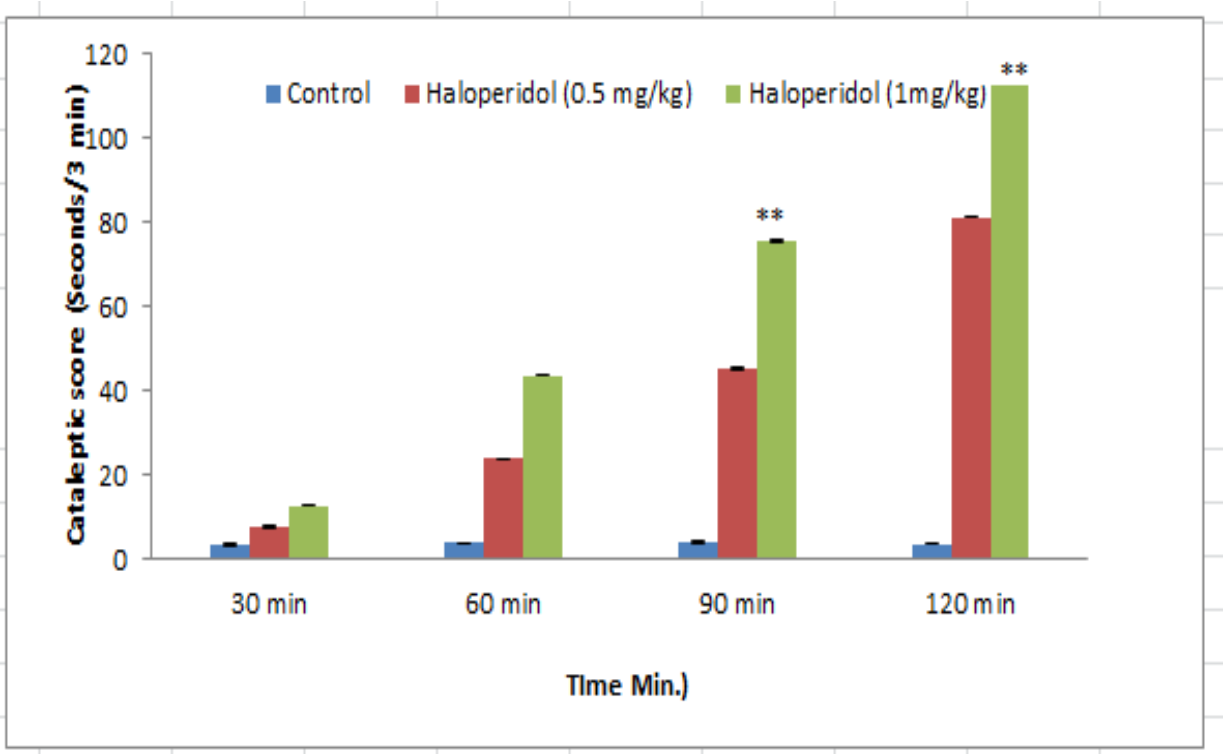
Effect of Haloperidol administration in rat on BAR test

To test of catalepsy, animals were positioned so that their hindquarters were on the bench, and their forelimbs rested on a 1 cm diameter horizontal bar, 6–9 cm above the bench. The length of time that animal maintained this position was recorded by stopwatch to a maximum of 180 s (mean of three consecutive trials; interval: 1 min). Animals would determine judge to be cataleptic if they maintained this position for 30 s or more.

Table 1: Effect of haloperidol on Cataleptic score in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.50 ± 0.09	3.84 ± 0.15	3.76 ± 0.06	3.71 ± 0.08
Haloperidol (0.5mg/kg)	7.50 ± 0.12	23.81 ± 0.12	45.47 ± 0.07*	81.36 ± 0.11*
Haloperidol (1mg/kg)	12.79 ± 0.11	43.62 ± 0.17	75.59 ± 0.06**	113.27 ± 0.12**

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control Group



*P <0.05, **P <0.01 compared to respective control group

Figure 1: Effect of haloperidol on Cataleptic score in Bar Test

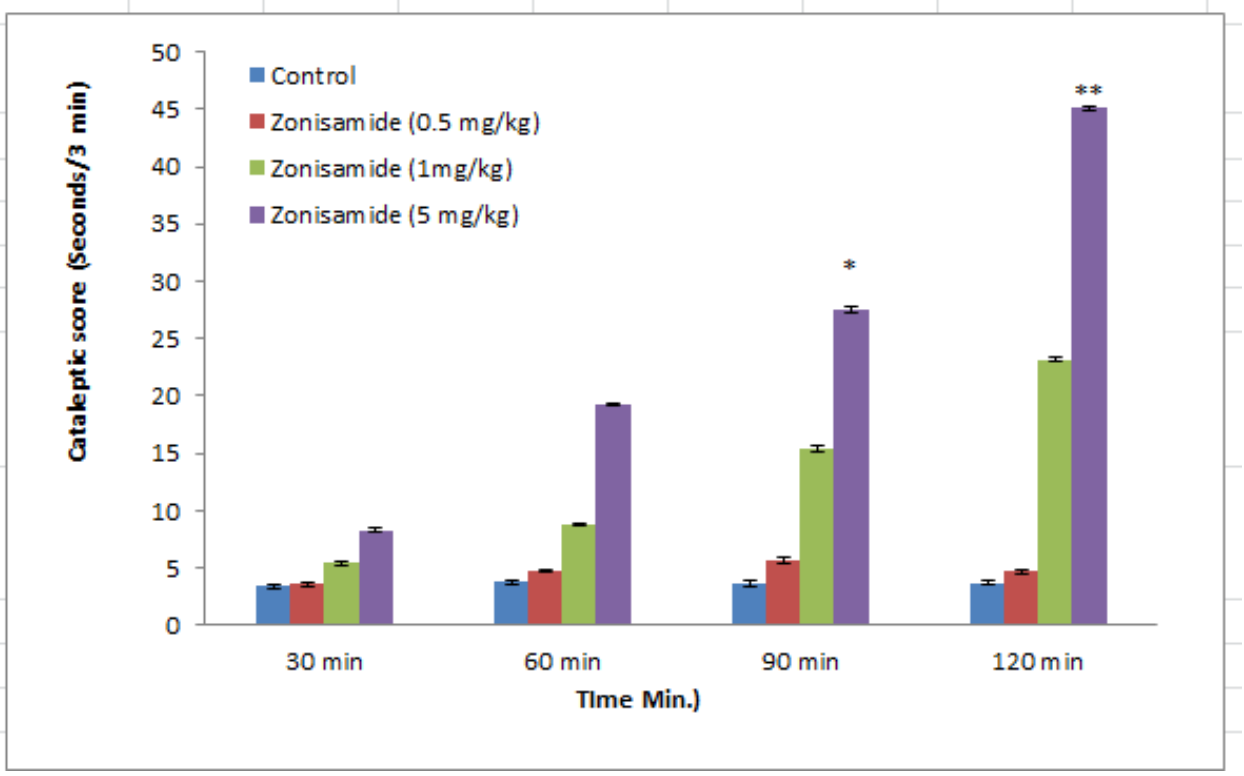
The end point of catalepsy was considered to occur when both front paws were removed from the bar or if the animal moved its head in an exploratory manner. The results confirmed that when animals in received were submitted to the catalepsy bar test catalepsy was evident.

Effect of Zonisamide administration in rat on BAR test

Table 2: Effect of zonisamide on Cataleptic score in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.42 ± 0.07	3.75 ± 0.12	3.62 ± 0.07	3.68 ± 0.09
Zonisamide (0.5mg/kg)	3.61 ± 0.08	4.79 ± 0.12	5.65 ± 0.09	4.69± 0.07
Zonisamide (1mg/kg)	5.41± 0.12	8.81 ± 0.12	15.47 ± 0.07	23.14 ± 0.11*
Zonisamide (5 mg/kg)	8.27 ± 0.11	19.32 ± 0.17	27.47 ± 0.06*	45.12 ± 0.08**

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control group



*P <0.05, **P <0.01 compared to respective control group

Figure 2: Effect of zonisamide on Cataleptic score in Bar Test

At low dose Zonisamide (0.5 mg/kg) does not produce any significant difference from normal control animals administered with saline. Zonisamide (1mg/kg) produce some effect in term of increasing descent latency time.At high dose Zonisamide (5 mg/kg) produce catalepsy in extent but less than haloperidol.

Effect of citral on Bar test

Citral, a monoterpene aldehyde, has sedative and muscle relaxant effects, and may be involved in vasorelaxation. Catalepsy, a state of behavioral immobility, can be induced by certain drugs or conditions, but the connection to citral specifically is not well-established.

The drug injected was Citral,, administered subcutaneously in the nape of the neck at a dose of 5 mg/kg, 10 mg/kg and 20 mg/kg. A saline solution was used as a vehicle.

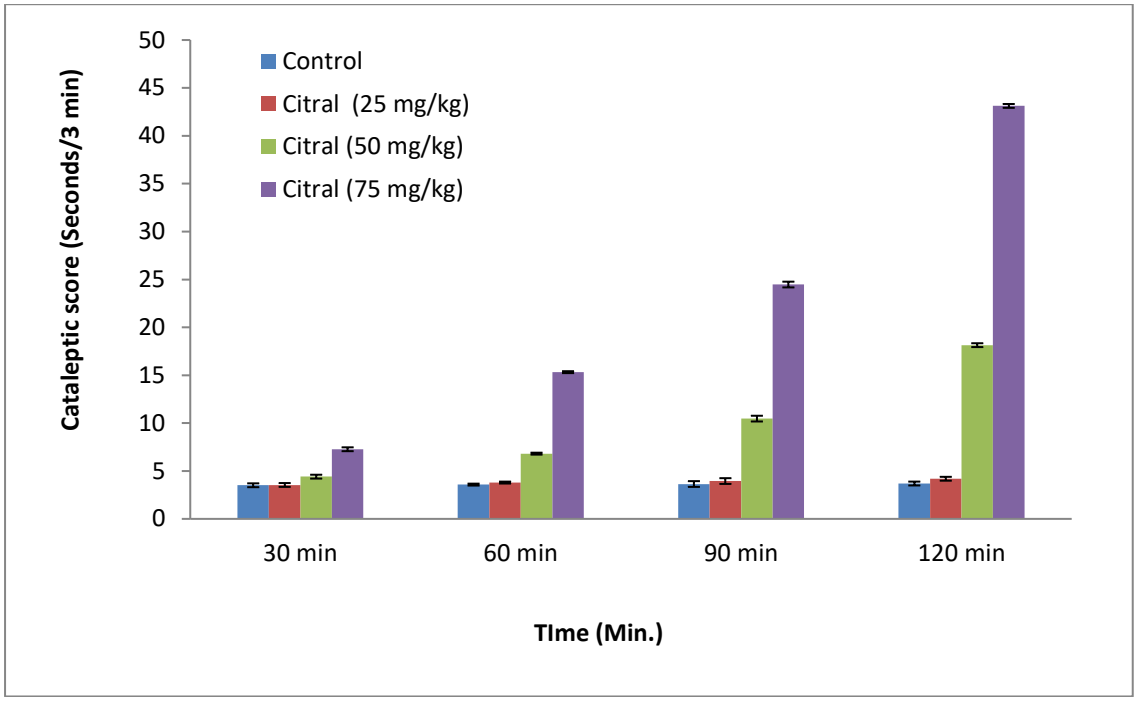
Experimental design Rats were divided into three group with six animal in each. The first group received an oral dose of vehicle (5ml/kg), second group received (Citral 25 mg/kg), third group received (Citral 50 mg/kg), fourth group (Citral 75 mg/kg) received the animal were divided into six groups (n = 6) and treated with respective test solutions as given below. The time it takes for the animal to remove one or both paws from the bar is recorded, with longer times indicating a higher degree of catalepsy.

Effect of citral administration in rat on BAR test

Table 3: Effect of citral on Cataleptic score in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.51 ± 0.06	3.58 ± 0.09	3.64 ± 0.08	3.69 ± 0.11
Citral (25 mg/kg)	3.54 ± 0.08	3.79 ± 0.02	3.95 ± 0.06	4.19± 0.08
Citral (50 mg/kg)	4.41± 0.12	6.81 ± 0.12	10.47 ± 0.07	18.14 ± 0.11
Citral (75 mg/kg)	7.27 ± 0.11	15.32 ± 0.17	24.47 ± 0.06	43.12 ± 0.08*

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control group



*P <0.05, **P <0.01 compared to respective control group

Figure 3: Effect of citral on cataleptic score in Bar Test

Citral 25 mg/kg and 50 mg/kg do not produce any significant difference from normal control animals administered with saline. Citral (75mg/kg) produces cataleptic effect in term of increasing cataleptic score and descent latency time in comparison to control group. The degree of catalepsy was measured at 30, 60, 90 and 120 and 240 min after haloperidol administration by using a method of standard bar test. Citral 25 mg/kg and 50 mg/kg do not produce any significant difference from normal control animals administered with saline. Citral (75mg/kg) produces cataleptic effect in term of increasing cataleptic score and descent latency time in comparison to control group.

Effect of Serotonin analogue antagonist (Glemanserin and Ritanserin) on Haloperidol induced cataleptic effect

Glemanserin (developmental code name MDL-11,939) is a drug which acts as a potent and selective 5-HT2A receptor antagonist. Ritanserin is a serotonin receptor antagonist, specifically targeting 5-HT2A and 5-HT2C receptors.

Table 4: Effect of Serotonin analogue antagonist on Haloperidol induced cataleptic effect on Descent latency in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.51 ± 0.06	3.58 ± 0.09	3.64 ± 0.08	3.69 ± 0.11
Haloperidol (1 mg/kg) + ritanserin (10 mg/kg)	14.79 ± 0.11	49.62 ± 0.17	81.59 ± 0.06*	124.27 ± 0.12**
Haloperidol (1 mg/kg) + Glemanserin (1 mg/kg)	29.27 ± 0.11	68.32 ± 0.17	108.47 ± 0.06*	153.12 ± 0.08**

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control group

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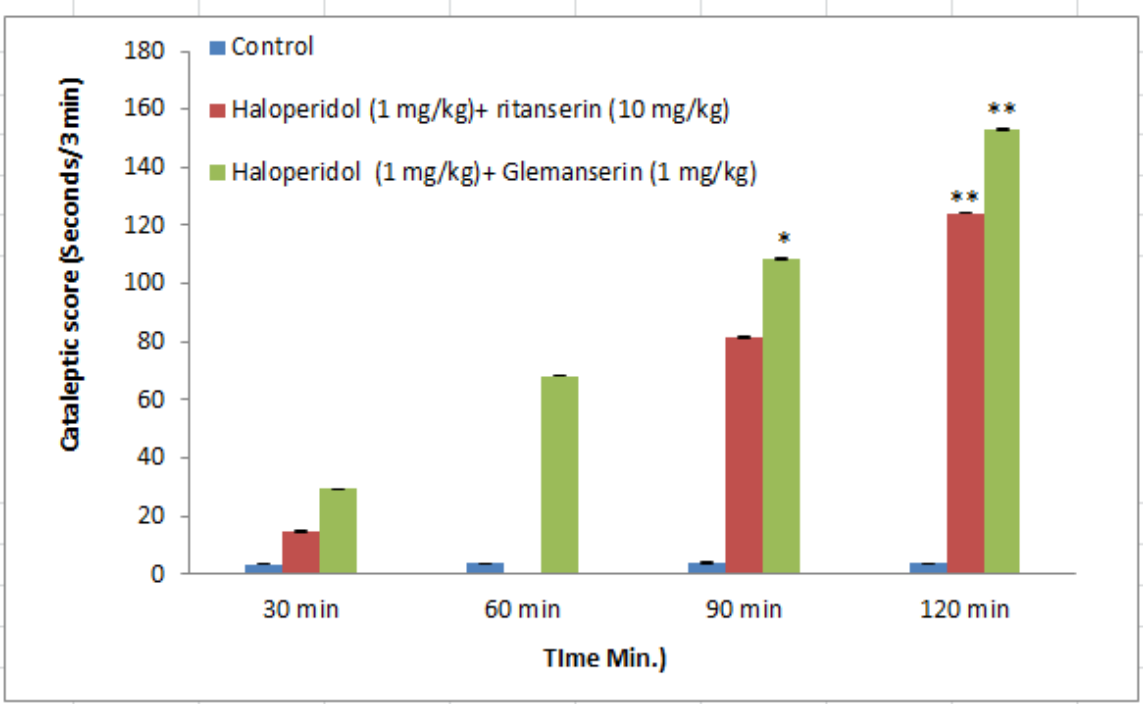

Figure 4: Effect of Serotonin analogue antagonist on Haloperidol induced cataleptic effect on Descent latency in Bar Test

Selective 5-HT2A receptor antagonist Glemanserin (MDL-11,939) at low dose (1 mg/kg) potentiate Haloperidol induced cataleptic effect in animals. 5-HT2A/2C antagonist ritanserin at high dose (10 mg/kg) cause potentiate Haloperidol induced cataleptic effect

Effect of Serotonin analogue agonist (Ipsapirone and Haloperidol) administration on rat in Bar Test

Table 5: Effect of Serotonin analogue agonist (Ipsapirone and Haloperidol) on on rat in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.51 ± 0.06	3.58 ± 0.09	3.64 ± 0.08	3.69 ± 0.11
Haloperidol (1 mg/kg) + Ipsapirone (5 mg/kg)	13.79 ± 0.04	9.62 ± 0.07	6.59 ± 0.06	5.27 ± 0.02**
Haloperidol (1 mg/kg) + RU 24969 (5 mg/kg)	23.27 ± 0.01	15.32 ± 0.02	12.47 ± 0.06	9.12 ± 0.08**

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control group

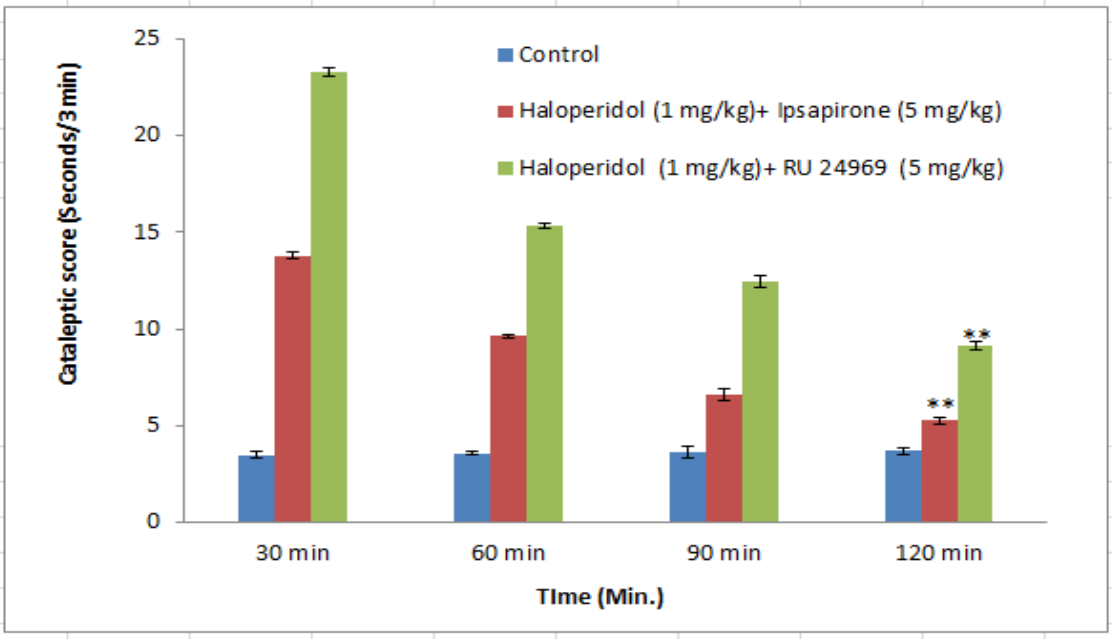

Figure 5: Effect of Serotonin analogue agonist on Haloperidol induced cataleptic effect Cataleptic score in Bar Test

In bar tests, RU 24969 has been shown to increase the number of bar presses, likely due to its agonistic effects at 5-HT1A/1B receptors, which can lead to increased locomotor activity. Ipsapirone (5 mg/kg) a selective 5-HT1A receptor agonist reverse the haloperidol induced cataleptic effect in animals and increase the locomotor activity.

Effect of Dopamine analogue Agonist (Ropinirole and Pramipexole) administration on rat in bar test

Table 6: Effect of Dopamine analogue Agonist (Ropinirole and Pramipexole) in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.51 ± 0.06	3.58 ± 0.09	3.64 ± 0.08	3.69 ± 0.11
Ropinirole (5 mg/kg)	3.79 ± 0.04	3.62 ± 0.07	3.59 ± 0.06	3.27 ± 0.02
Pramipexole (5 mg/kg)	3.27 ± 0.01	3.32 ± 0.02	3.47 ± 0.06	3.12 ± 0.08

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control group

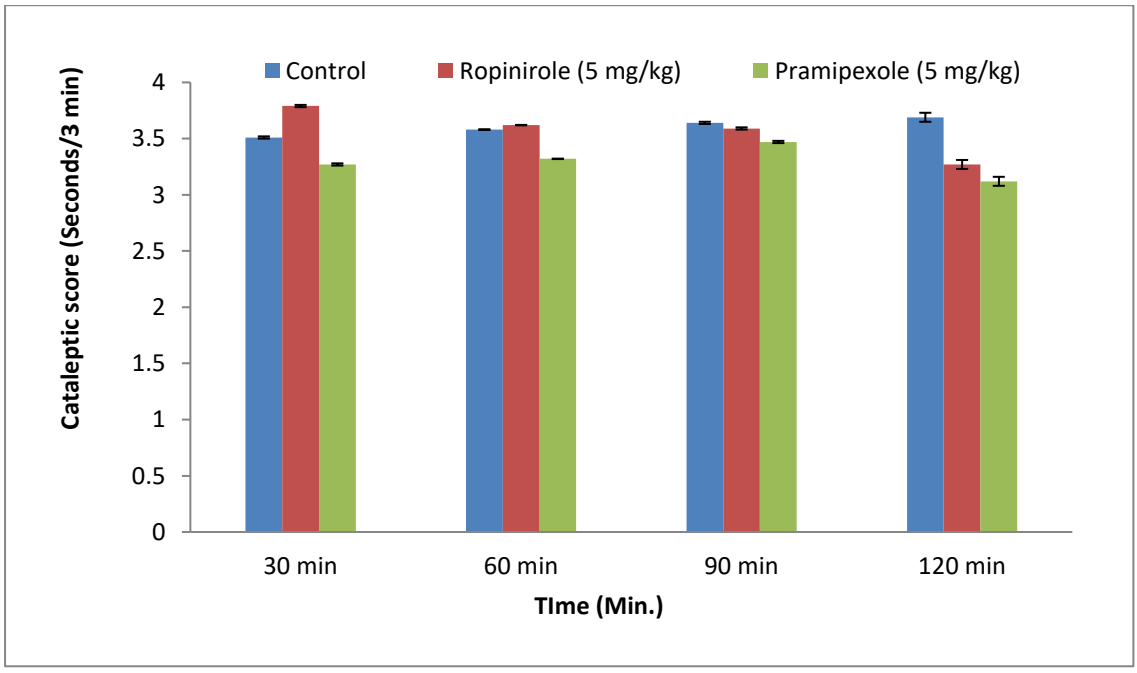

Figure 6: Effect of Dopamine analogue Agonist in Bar Test

Dopamine analogue Agonist showed results similar to normal control group. They do not produce catalepsy.

Effect of Dopamine analogue antagonists (Raclopride and Haloperidol) on rat in Bar Test

Table 7: Effect of Dopamine analogue antagonists on Cataleptic score in Bar Test

Treatment	Cataleptic score (Seconds/3 min)			
	30 min	60 min	90 min	120 min
Control	3.50 ± 0.09	3.84 ± 0.15	3.76 ± 0.06	3.71 ± 0.08
Haloperidol (1mg/kg)	12.79 ± 0.11	43.62 ± 0.17*	75.59 ± 0.06**	113.27 ± 2.12**
Raclopride (2 mg/kg)	10.79 ± 0.05	41.62 ± 1.13	71.09 ± 2.02**	107.15 ± 2.28**

Values are mean ± SEM (n=6); *P <0.05, **P <0.01 compared to respective control group

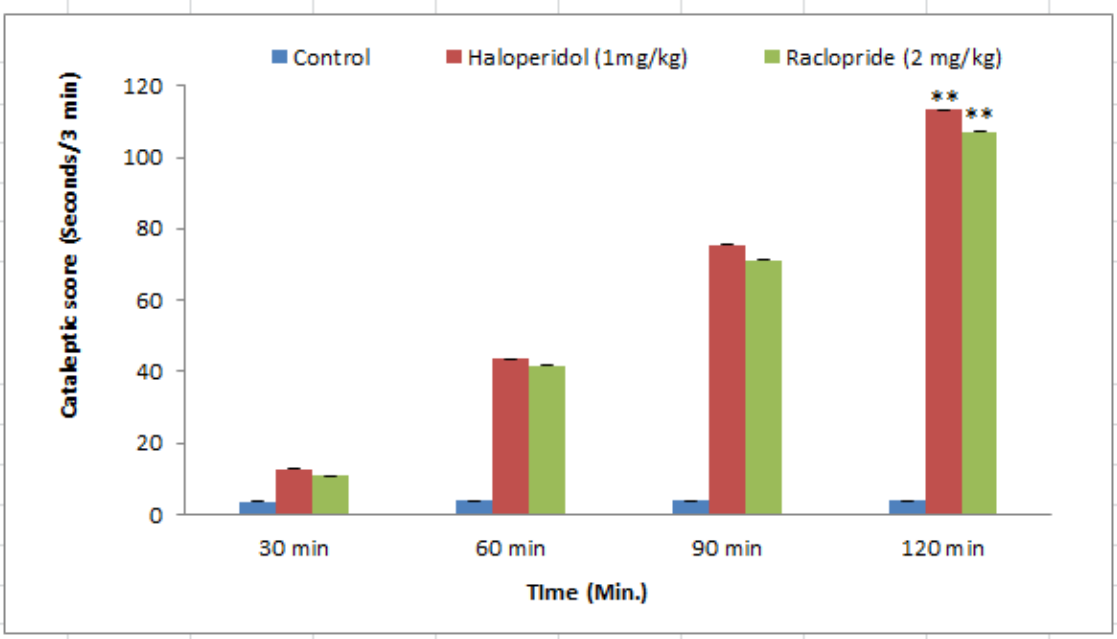

Figure 7: Effect of Dopamine analogue antagonists on Cataleptic score in Bar Test

DISCUSSION

BAR Test

Catalepsy is a condition characterized most often by rigidity of extremities and by decreased sensitivity to pain. It is understood as a behavioural state in animals in which the animal cannot rectify externally imposed postures. This model is depictive of the extrapyramidal side effects induced in neurodegenerative disorders such as Parkinson's disease by blockade of the dopamine receptors localized postsynaptically in the striatum. Typical antipsychotics such as haloperidol have been shown to exhibit similar effects by blocking the dopaminergic action in the nigro-striatal pathway leading to high frequency of extrapyramidal-motor side effects such as dystonias, pseudoparkinsonism, etc.

Effect of Haloperidol administration on rats in Bar test

Haloperidol causes dysfunctioning of various neurotransmitters such as acetylcholine, GABA, and serotonin. Pathology of haloperidol induced catalepsy underlying increased oxidative stress. Haloperidol, an antipsychotic drug, blocks central dopamine receptor in striatum. It also produces a behavioral state in rats in which they fail to correct externally imposed postures (called catalepsy); thus, keeping the above fact in mind, the haloperidol induced catalepsy model. Haloperidol is a well-known neuroleptic, primarily acting as a D2 receptor antagonist in the mesolimbic-mesocortical pathway. Due to its non-selective action, it also produces blockade of post-synaptic D2 receptors in the nigrostriatal pathway leading to the development of extrapyramidal side effects in humans and catalepsy in animals. Haloperidol induced catalepsy is also associated with an increase in oxidative stress in the brain

A relevant aspect of our procedure is related to the time interval between the drug administration and the registration of catalepsy. Different studies have evaluated the intensity of catalepsy using various intervals from haloperidol administration to response recording. In our experiment, the use of a 30-min interval between drug administration and the different tests is determined To get an index of catalepsy we used the bar test, a widely used procedure in previous research in this field.

Especially relevant for interpreting our results is the fact that the neurochemical response produced by haloperidol is related to the dose administered. Specifically, a low dose of haloperidol has been observed to have an antagonist effect on presynaptic autoreceptors without affecting somatodendritic (postsynaptic) receptors, while a higher dose block both types of receptors. Considering these mechanisms, we can offer an explanation, albeit speculative, of the results obtained in our experiment: The presence of the context associated with haloperidol would induce a CR that would initially be similar to that produced by the relatively high dose of drug injected in the test phase (0.5 mg/kg), blocking both autoreceptors and postsynaptic receptors and, consequently, inducing the conditioned catalepsy effect. However, the CR would decrease in intensity over time, in such a way that it would mimic the effect produced by a low dose of the drug. Therefore, the activity of the postsynaptic receptors would normalize, responding to the excess of dopamine accumulated by blockage of the autoreceptors, leading to the conditioned increase in locomotor activity.

Effect of Zonisamide administration on rats in Bar test

Zonisamide is a sulfonamide anticonvulsant used as an adjunctive therapy in adults with partial-onset seizures. Zonisamide may act by blocking repetitive firing of voltage-gated sodium channels, leading to a reduction of T-type calcium channel currents or by binding allosterically to GABA receptors. Zonisamide is an Anti-epileptic Agent. The drug injected was Zonisamide, administered subcutaneously in the nape of the neck at a dose of 0.5 mg/kg, 1mg/kg and 5 mg/kg. A saline solution was used as a vehicle.

The degree of catalepsy was measured at 30, 60, 90 and 120 and 240 min after Zonisamide administration by using a method of standard bar test. The end point of catalepsy was considered to occur when both front paws were removed from the bar or if the animal moved its head in an exploratory manner. Mean descent latency for catalepsy test during conditioning as a function of the drug injected before and after each experimental session. At low dose Zonisamide (0.5 mg/kg) does not produce any significant difference from normal control animals administered with saline. Zonisamide (1mg/kg) produce some effect in term of increasing descent latency time. At high dose Zonisamide (5 mg/kg) produce catalepsy in extent but less than haloperidol.

Effect of citral administration on rats in Bar test

Citral, a monoterpene aldehyde, has sedative and muscle relaxant effects, and may be involved in vasorelaxation. Catalepsy, a state of behavioral immobility, can be induced by certain drugs or conditions, but the connection to citral specifically is not well-established. Citral, is a part of the essential oil of several medicinal plants, is generally regarded as safe for human and animal consumption. Studies have introduced citral as a functional component of some essential oils in anxiolytic and antidepressant therapies The drug injected was Citral, administered subcutaneously in the nape of the neck at a dose of 5 mg/kg, 10 mg/kg and 20 mg/kg. A saline solution was used as a vehicle. Citral 25 mg/kg and 50 mg/kg do not produce any significant difference from normal control animals administered with saline. Citral (75mg/kg) produces cataleptic effect in term of increasing cataleptic score and descent latency time in comparison to control group.

Effect of Serotonin analogue antagonist (Glemanserin and Ritanserin) Haloperidol administration on rats in Bar test

Glemanserin (developmental code name MDL-11,939) is a drug which acts as a potent and selective 5-HT2A receptor antagonist. The first truly selective 5-HT2A ligand to be discovered, glemanserin resulted in the development of the widely used and even more potent and selective 5-HT2A receptor antagonist volinanserin (MDL-100,907), which is a fluorinated analogue. Ritanserin is a serotonin receptor antagonist, specifically targeting 5-HT2A and 5-HT2C receptors. It was investigated as a potential treatment for conditions like anxiety, depression, schizophrenia, and insomnia, but was never marketed for clinical use. Research has explored its effects on sleep, alcohol dependence, and various psychiatric symptoms. Selective 5-HT2A receptor antagonist Glemanserin (MDL-11,939) at low dose (1 mg/kg) potentiate Haloperidol induced cataleptic effect in animals. 5-HT2A/2C antagonist ritanserin at high dose (10 mg/kg) cause potentiate Haloperidol induced cataleptic effect

Effect of Serotonin analogue agonist (Ipsapirone and RU 24969) on Haloperidol induced cataleptic effect

RU 24969 is a 5-HT1A and 5-HT1B receptor agonist that has been used in various studies to investigate its effects on behavior, particularly locomotor activity. In bar pressing tests, RU 24969 has been shown to increase the number of bar presses, likely due to its agonistic effects at 5-HT1A/1B receptors, which can lead to increased locomotor activity. Ipsapirone (5 mg/kg) a selective 5-HT1A receptor agonist reverse the haloperidol induced cataleptic effect in animals and increase the locomotor activity. RU 24969 is a 5-HT1A and 5-HT1B receptor agonist reverse the haloperidol induced cataleptic effect in animals and increase the locomotor activity but showed less effect than Ipsapirone.

Effect of Dopamine analogue Agonist (Ropinirole and Pramipexole)

Dopamine is one of the neurotransmitters that has crucial role in brain functions. In particular, locomotor activity can be differentially regulated by biological conditions contributing to dopamine status in brain. Dopamine agonists can antagonize catalepsy, a state of rigidity and immobility, induced by dopamine antagonists. This is because dopamine agonists stimulate dopamine receptors, effectively counteracting the blocking effect of dopamine antagonists on these receptors.

Ropinirole has a high affinity for post-synaptic dopamine receptors in the central and peripheral nervous systems. The dopamine receptors (D2) are G-protein-coupled inhibitory neurons located primarily in the striatonigral, mesolimbic, and tuberoinfundibular systems. They inhibit adenylyl cyclase and calcium channels and activate potassium channels.

Pramipexole is a dopamine agonist that works by stimulating dopamine receptors in the brain, which can improve motor function in Parkinson's disease models. Pramipexole is used to treat Parkinson disease. It may be used alone or in combination with other medicines (eg, levodopa). Pramipexole is a dopamine agonist that works on the nervous system to help treat the symptoms of Parkinson disease. Pramipexole is also used to treat Restless Legs Syndrome (RLS). RLS is a neurologic disorder that affects sensation and movement in the legs and causes the legs to feel uncomfortable. This results in an irresistible feeling of wanting to move your legs to make them comfortable. Dopamine analogue Agonist showed results similar to normal control group. They do not produce catalepsy.

Effect of Dopamine analogue antagonists (Raclopride and haloperidol) on Cataleptic score in Bar Test

Raclopride is a typical antipsychotic. It acts as a selective antagonist on D2 dopamine receptors. It has been used in trials studying Parkinson Disease. Its selectivity to the cerebral D2 receptors. DA D2 receptor antagonist haloperidol or raclopride produce catalepsy.

CONCLUSION

Catalepsy is a condition characterized most often by rigidity of extremities and by decreased sensitivity to pain. It is understood as a behavioural state in animals in which the animal cannot rectify externally imposed postures. BAR Test model is depictive of the extrapyramidal side effects induced in neurodegenerative disorders such as Parkinson's disease by blockade of the dopamine receptors localized postsynaptically in the striatum. Haloperidol is a well-known neuroleptic, primarily acting as a D2 receptor antagonist in the mesolimbic-mesocortical pathway. Due to its non-selective action, it also produces blockade of post-synaptic D2 receptors in the nigrostriatal pathway leading to the development of extrapyramidal side effects in humans and catalepsy in animals.

Blocking dopamine receptors with neuroleptic drugs can induce catalepsy, a state of akinesia and rigidity very similar to that seen in Parkinson's disease. Haloperidol is a dopamine D2 receptor antagonist that induces catalepsy when systemically administered to rodents. Different serotonin receptors (5-HT1A, 5-HT2A, 5-HT3) and their agonists/antagonists can have differing effects on catalepsy. For instance, 5-HT1A receptor agonists can antagonize raclopride-induced catalepsy, while antagonists may enhance it.

At high dose Zonisamide (5 mg/kg) produce catalepsy in extent but less than haloperidol. Citral 25 mg/kg and 50 mg/kg do not produce any significant difference from normal control animals administered with saline. Citral (75mg/kg) produces cataleptic effect in term of increasing cataleptic score and descent latency time in comparison to control group. Selective 5-HT2A receptor antagonist Glemanserin (MDL-11,939) at low dose (1 mg/kg) potentiate Haloperidol induced cataleptic effect in animals. 5-HT2A/2C antagonist ritanserin at high dose (10 mg/kg) cause potentiate Haloperidol induced cataleptic effect Ipsapirone (5 mg/kg) a selective 5-HT1A receptor agonist reverse the haloperidol induced cataleptic effect in animals and increase the locomotor activity. RU 24969 is a 5-HT1A and 5-HT1B receptor agonist reverse the haloperidol induced cataleptic effect in animals and increase the locomotor activity but showed less effect than Ipsapirone.

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