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EVALUATION OF ANTIPSYCHOTIC AND ANXIOLYTIC ACTIVITY OF ALOE VERA (ALOE BARBADENSIS MILLER) IN RATS

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ABSTRACT

In recent years, there has been much focus on the apparent heterogeneity of schizophrenic symptoms. By contrast, this article proposes a unifying account emphasizing basic abnormalities of consciousness that underlie and also antecede a disparate assortment of signs and symptoms. Schizophrenia, is fundamentally a self-disorder or ipseity disturbance is characterized by complementary distortions of the act of awareness, hyper reflexivity and diminished self-affection. Anxiety impacts people in ways that they are unaware. In the presence of anxiety, attention is highly directed towards threatening information. Recently, anxiety was found to impact task switching performance when threatening stimuli were present. In the current study, we examined the Anxiolytic and antipsychotic activity of *Aloe vera* (*Aloe barbadensis miller*) in rats. This study reveals that the *Aloe vera* has showed decreased effects of turning behaviour, weaving behaviour, head bobbing and falling behaviour. It also showed decreased effect of loco motor activity and increase in catalepsy scoring. Thus it shows anti psychotic and anti anxiety effects.

KEYWORDS: Schizophrenia, Anxiety, Aloe vera.

1. INTRODUCTION

Schizophrenia

Schizophrenia is chronic, severe mental disorder caused by some inherent dysfunction of brain that has affected people throughout the history, resulting from abnormalities that arises

early in life and disrupt normal development of the brain and has a lifetime risk of 1% and affects at all age groups, approximately 10% die from suicide. The evidence implies that neurodevelopmental abnormalities contribute to susceptibility to schizophrenia. Firstly, clinical studies show that patients with schizophrenia manifest minor behavioral abnormalities in childhood even before the onset of schizophrenia.

Secondly, recent advanced imaging techniques such as magnetic resonance imaging provide reliable evidence of abnormalities during development of the central nervous system.Such abnormalities include consistent increases in ventricular size at the onset of schizophrenia, with notable alterations in some areas including the prefrontal cerebral cortex and hippocampus.

The acute psychotic schizophrenic patients will respond usually to antipsychotic medication.
Phenothiazines: [ex: chlorpromazine, fluphenazine, and thioridazine].

Chlorpromazine is a low potency prototype agent which acts as antagonist of d2 dopamine receptors in the mesolimbic system of the brain.

Thioxanthenes: [ex: flupenthixol, clopenthixol]
Flupenthixol is use by blocking postsynaptic dopamine receptors in the brain and they also produce an alpha adrenergic blocking effect and depress release of hypothalamic and hypophyseal hormones.

Butyrophenones: [ex: haloperidol, droperidol] haloperidol a Butyrophenones, apparently owes its antipsychotic effect primarily to its antagonistic activity on dopamine D2-receptors in the central nervous system. Compared to other agent it has a relatively mild sedative effect but it often causes extra pyramidal symptoms. It has an antiemetic effect through its activity in the 'chemoreceptor trigger zone'. Antagonistic effects on other receptors (e.g. histamine or serotonin receptors) have marginal importance.

Atypical drugs: [Ex: Clozapine, Risperidone, Olanzapine]
Clozapine is a first atypical antipsychotic agent with week d2 blocking action with no extra pyramidal effects.

Olanzapine is use in blocking multiple monoaminergic [D2, 5-HT2] as well as muscuranic and H1 receptors. Both +ve &-ve symptoms are improved.[1]

Anxiety

Anxiety is a emotional state associated with fear or worry. The source of this uneasiness is not always known or recognized, which can add to the distress you feel. Some people suffer a lot of anxiety over a long period of time which controls them and makes their lives difficult. These conditions are called anxiety disorders and can be treated by therapy and medicine.

Aloe vera (Aloe barbadensis miller)

Aloe vera (*Aloe barbadensis Miller*) is a member of the lilacae family. It is native to tropical and southern Africa. It has been cultivated for its thick exudates that contain many active compounds with known therapeutic properties. The extracts have been found to reduce oxygenase activity and relieve inflammation.[2] In other aloe species of Aloe the active phenolic compounds were most concentrated in the peripheral regions of the plant leaves[3] The top third of the leaf and the leaf edges have the highest concentration because those parts are most susceptible to consumption by herbivores.[4]

As a drink it protects the mucous membrane of the stomach especially when irritated or damaged. Aloe vera juice is considered helpful for relieving many types of gastrointestinal irritation and juice products are widely available. In Germany, concentrated extracts of dried Aloe leaves are used as laxative preceeding rectal surgery and as a hemorrhoid treatment. Aloe gel is perhaps the most widely recognized herbal remedy in the United State today; it is used to relieve thermal burn, sunburn and promote wound healing. In addition, research suggests that Aloe gel can help stimulate the body's immune system.[5] Leaves of Aloe vera acts as for alternative or complementary medicine as a cardio tonic agent.[6]

2. MATERIALS AND METHODS

The collected plant material was washed with hot water and cut them into pieces, collected in a beaker, kept boiling for two hours by adding some amount of distilled water, filter it, collect the filtrate and cool it, then add chloroform to it in a separating funnel, collect the chloroform extract and the chloroform extract was taken in a china dish and evaporated. The dried extract of Aloe vera was collected and stored. This dried extract contains the active compound aloe emodin-8-O-glycoside (AEG).[7]

Animals

Twenty rats weighing (170 ± 5 g) were taken and maintained under standard laboratory conditions in an air conditioned room and housed in stainless steel cages four per cage at

temperature 23±5 ºc. The animal diet was given. Animals were acclimatized for one week prior to experiment.

Drugs

Haloperidol, Olanzapine, Ketamine are collected from local pharmacy at karimnagar.

Catalepsy Scoring

The rats were weighed and grouped as standard, test, control and were treated with Haloperidol (5mg/kg, p.o), EASA (650 mg/kg, p.o) and CMC (1%, p.o) respectively. The fore paws of the rats were placed on a wooden bar elevated at 9cm above the ground. Duration for which the animal maintained the imposed posture was noted as the time required for removing the fore paws from the bar. Duration of catalepsy was measured at 0, 30, 60, 90,120 min and was assessed by scoring technique.

Pole Climbing Test

A chamber which consist a 2.8 kHz speaker situated on the top, stainless steel pole 2.5cm in diameter is suspended, and condition stimulus (buzzer sound) is given for 10seconds, followed by an unconditional stimulus-a scrambled shock delivered to the grid floor. Animals were trained to avoid the unconditional response (shock) following the conditional stimulus.

The rats were weighed and grouped as standard, test, control and were treated with Haloperidol (5mg/kg, p.o), Aloe vera (5mg & 10mg/kg, p.o) and CMC (1%, p.o). The conditioned stimulus was given for 10 seconds and unconditioned stimulus, foot shock delivered through the grid of floor applied for 10 seconds. Animals kept in the chamber jumped on the pole on hearing the buzzer tone to avoid electric shock. Failure to do so result in foot shock applied for 10 seconds.5 trials were conducted. The latency period to climb the pole was noted for standard, Aloe vera and control treated group.

Ketamine-Induced Stereotypic Behaviour in Mice

Animals were divided into five groups and each group consisted of four animals. The control animals received normal diet and treated with Ketamine (50 mg/kg) for 15 consecutive days. The animals of standard groups received Olanzapine (5 mg/kg) after 30 min Ketamine was given, (50 mg/kg) for 15 consecutive days. The animals of test groups received different Aloe vera (5mg & 10mg/kg, p.o) through a specially prepared diet and after 30 min Ketamine was given (50 mg/kg) for 15 consecutive days. Each rat was individually placed into plastic cages

(37 × 24 × 30 cm3) divided into quadrants by lines on the floor and allowed to acclimatize for at least 30 min before the testing began. Behavioural tests were performed between 10 a.m. and 4 p.m. The stereotypic behaviour was assessed by counting the number of turning, weaving, head-bobbing and ataxia. Turning was measured by counting turn around every 15 min over 60 min. Weaving and head-bobbing were measured by counting its neck wave right and left, and go up and down every 15 min over 60 min. Ataxia was assessed by counting the number of falls of each rat on the floor of the cage every 15 min over 60 min period.

3. RESULTS

Locomotory Activity

Table 2: *Aloe vera* on loco motor activity (actophotometer) in rats at different time intervals (min).

Groups	Treatment	Photocell Counts			
		30min	% Inhibition	60min	% Inhibition
I	Control (3%Tween 80) (p.o.)	458.11±3.18		456.32±6.24	
II	Diazepam (3 mg / kg) (p.o.)	105.43±0.13**	78.02%	103.62±0.91**	73.12%
III	*Aloe vera* (5 mg / kg) (p.o.)	115.09±1.33**	74.87%	114.08±3.11**	75.01%
IV	*Aloe vera* (10 mg / kg) (p.o.)	109.14±3.91**	76.18%	106.51±4.15**	76.66%

(Observation period: 10 min for all parameters) Values are expressed as mean ± SEM, from 6 mice. Significant at **P< 0.01 as compare to control using One way ANOVA followed by followed by Dennett's *t*-test.).

Stereotypic Behaviour

Turning Behaviour of Rats

Table 3: Effect of Aloe vera (5mg & 10mg/kg, p.o) on Turning behaviour in rats at different time intervals (min).

Groups	Treatment	Turning behaviour			
		15min	30min	45min	60min
I	Control +Ketamine (50mg/kg *i.p.)*	21.51±1.09	16.92±3.13	14.31±1.83	13.62±1.85
II	Olanzapine (5mg/kg i.p.) + Ketamine (50mg/kg *i.p.)*	11.99±2.15	10.62±1.66	11.53±2.16	12.79±1.90
III	*Aloe vera* (5 mg / kg) (p.o.)	16.44±1.09	14.24±1.19	13.22±1.81	11.99±1.44
IV	*Aloe vera* (10 mg / kg) (p.o.)	17.15±1.86	13.11±1.86	11.16±1.43	10.19±1.81

(Observation period: 10 min for all parameters) Values are expressed as mean ± SEM, from 6 mice. Significant at **P< 0.01 as compare to control using One way ANOVA followed by followed by Dennett's *t*-test.)

Weaving Bahaviour of Rats

Table 4: Effect of Aloe vera (5mg & 10mg/kg, p.o) on weaving behaviour in rats at different time intervals (min).

Groups	Treatment	Weaving behaviour			
		15min	30min	45min	60min
I	Control +Ketamine (50mg/kg *i.p.)*	11.01±2.06	11.62±1.13	12.11±1.33	12.66±1.81
II	Olanzapine (5mg/kg i.p.) + Ketamine (50mg/kg *i.p.)*	4.91±0.12	4.61±0.16	4.03±0.19	4.19±0.11
III	*Aloe vera* (5 mg / kg) (p.o.)	8.13±1.15	8.01±1.13	7.04±1.91	7.13±0.15
IV	*Aloe vera* (10 mg / kg) (p.o.)	6.13±0.11	5.91±0.34	5.81±0.16	5.13±0.59

(Observation period: 10 min for all parameters) Values are expressed as mean ± SEM, from 6 mice. Significant at **P< 0.01 as compare to control using One way ANOVA followed by followed by Dennett's *t*-test.).

Head Bobbing Behaviour of Rats

Table: 5 Effect of Aloe vera (5mg & 10mg/kg, p.o) on Head-Bobbing in rats at different time intervals (min).

Groups	Treatment	Head-Bobbing			
		15min	30min	45min	60min
I	Control +Ketamine (50mg/kg *i.p.)*	20.59±2.01	17.12±1.13	15.11±1.83	14.12±1.75
II	Olanzapine (5mg/kg i.p.) + Ketamine (50mg/kg *i.p.)*	8.19±0.15	7.12±0.66	6.53±0.16	5.79±0.90
III	*Aloe vera* (5 mg / kg) (p.o.)	10.11±1.54	9.14±1.15	8.13±1.65	7.84±1.91
IV	*Aloe vera* (10 mg / kg) (p.o.)	9.14±0.91	8.14±0.15	7.13±0.61	6.11±0.83

(Observation period: 10 min for all parameters) Values are expressed as mean ± SEM, from 6 mice. Significant at **P< 0.01 as compare to control using One way ANOVA followed by followed by Dennett's *t*-test.).

Ataxia Behaviour of Rats

Table 6: Effect of Aloe vera (5mg & 10mg/kg, p.o) on Falling in rats at different time intervals (min).

Groups	Treatment	Falling			
		15min	30min	45min	60min
I	Control +Ketamine (50mg/kg *i.p.)*	11.04±1.05	9.12±1.93	8.11±1.43	7.66±1.41
II	Olanzapine (5mg/kg i.p.) + Ketamine (50mg/kg *i.p.)*	6.11±0.32	5.91±0.56	4.03±0.69	3.19±0.51
III	*Aloe vera* (5 mg / kg) (p.o.)	9.13±1.05	8.15±1.24	7.15±0.35	6.51±0.41
IV	*Aloe vera* (10 mg / kg) (p.o.)	8.04±0.09	7.09±0.45	6.08±0.35	5.01±0.91

(Observation period: 10 min for all parameters) Values are expressed as mean ± SEM, from 6 mice. Significant at **P< 0.01 as compare to control using One way ANOVA followed by followed by Dennett's *t*-test.).

Catalepsy Scoring

Table 7: Effect of Aloe vera (5mg & 10mg/kg, p.o) on Cataleptic score in rats at different time intervals (min).

Groups	Treatment	Cataleptic score				
		0min	30min	60min	90min	120min
I	Control (3%Tween 80) (p.o.)	0.81±0.03	0.19±0.03	0.21±0.01	0.63±0.02	0.24±0.04
II	Haloperidol (5 mg / kg) (p.o.)	0.80±0.01*	2.89±0.02*	2.89±0.01*	3.05±0.06*	3.21±0.01*
III	*Aloe vera* (5 mg / kg) (p.o.)	0.81±0.03*	1.59±0.04*	1.48±0.03*	1.65±0.03*	2.09±0.05*
IV	*Aloe vera* (10 mg / kg) (p.o.)	0.82±0.02*	1.19±0.03*	1.45±0.02*	1.51±0.02*	2.01±0.01*

(Observation period: 10 min for all parameters) Values are expressed as mean ± SEM, from 6 mice. Significant at **P< 0.01 as compare to control using One way ANOVA followed by followed by Dennett's *t*-test.).

4. DISCUSSION

Locomotor Activity, Stereotyoic Behaviour, Turning

Aloe vera at the dose of 5,10mg for 15 successive days showed significant (p<0.05) decrease in turning behaviour of mice induced by Ketamine. However at the concentration of 8% w/w BRJ remarkably (p<0.01) decreased the turning pattern of mice induced by Ketamine. Animals treated with Olanzapine (5 mg/kg, *i.p.*) decreased the turning behaviour.

Weaving Bahaviour of Rats

Weaving pattern was measured by counting its paw movements standing on hind legs every 15 min over 60 min period. 10mg *Aloe Vera* remarkably (p<0.01) decreased weaving pattern of mice produced by Ketamine. During 15 and 30 min BRJ 2% w/w showed remarkable (p<0.05) decrease in weaving pattern. 10mg *Aloe Vera* remarkably (p<0.01) decreased weaving pattern of mice produced by Ketamine at 30 min and reduction in weaving pattern was remarkable (p<0.05) 15, 45 and 60 min. Animals treated with Olanzapine (5 mg/kg, *i.p.*) decreased the weaving behaviour.

Head Bobbing Behaviour of Rats

5mg,10mg *Aloe Vera* for 15 successive days showed significant (p<0.05) decrease in head-bobbing pattern of mice produced by Ketamine. Administration of *Aloe Vera* at the 10mg for 15 successive days remarkably (p<0.01) reduced head-bobbing pattern of mice produced by Ketamine.

Ataxia Behaviour of Rats

5mg, 10mg *Aloe Vera* (p<0.05) reduced falling behaviour of mice at 15 and 30 min. Administration of BRJ 8% w/w remarkably (p<0.01) decreased falling behaviour of mice. There was no falling attempt shown by the standard and test drug at 60 min.

Catalepsy

The rats were weighed and grouped as standard, two groups of test, control and were treated with Haloperidol (5mg/kg, p.o), 5mg,10mg *Aloe Vera* and CMC (1%, p.o) respectively. The fore paws of the rats were placed on a wooden bar elevated at 9cm above the ground. Duration for which the animal maintained the imposed posture was noted as the time required for removing the thererefore paws from the bar. Duration of catalepsy was measured at 0, 30, 60, 90,120 min and was assessed by scoring technique of Costall and Naylor.

5. CONCLUSION

The *Aloe vera* (*Aloe barbadensis miller*) has showed decreased effects of turning behaviour, weaving behaviour, head bobbing and falling behaviour. It also showed decreased effect of loco motor activity and increase in catalepsy scoring. Thus it shows anti psychotic and anti anxiety effects.

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