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ANXIOLYTIC ACTIVITY OF *ALOE VERA* (L.) BURM.F TESTED IN RODENTS

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ABSTRACT:
Aloe vera was evaluated for CNS activities in mice and different behavioral activities for anxiety and depression were tested on Exploratory activity, Open field test, Swimming – induced Depression test, Stationary Rod, Cage Crossing and Inclined Plane test. *Aloe vera* was administered orally in both sexes of mice and was found to cause significant depression in general as well as exploratory behavioral profiles. The results revealed that *Aloe vera* caused reduction of Exploratory and Locomotor activities along with the significant decrease in traction in an inclined plane test. The results suggest that *Aloe vera* may have anxiolytic potential with sedative action.

Keywords: *Aloe vera*, anxiolytic , Exploratory activity, Locomotor activity, depression.

INTRODUCTION

Aloe vera (L.) Burm.f family *Liliacea* is a perennial plant (Rajasekaran *et al*., 2005) used as herbal medicine (Marshall., 2000) is a succulent plant (Ernst., 2000). Two different parts of *Aloe vera*, the leaf inner portion produces the mucilage or gel and the outer part just beneath the green rind of *Aloe vera* is a bitter pale yellow latex responsible for the purgative agent (Ramachandra and Rao., 2008) have been used traditionally. The total solid portion varies from 0.5 to 1.5%.

Different bioactive constituents, at least 75 are present in *Aloe vera* (Eshun., 2006, Joseph and Raj., 2010). The anti-inflammatory effect is present due to the presence of Carboxypeptidase which is responsible to inactivate the bradykinins (Ro *et al.,* 2000). Some other enzymes are also present in *Aloe vera* such as lipase, Catalase and amylase that can help in digestion. Anthraquinones are the bitter portion of *Aloe vera* and contain derivatives including Aloe – emodin (Yang *et al.,* 2003), Anthronol, Barbaloin, Isobarboloin that can act as laxative agents (Davis *et al.,* 2006). Sistosterol, Campesterol are the derivatives of Sterol found in *Aloe vera* which have the property to reduce the edema (Saritha and Anilakumar., 2011). Antioxidant vitamins are also found in *Aloe vera* including vitamin A, B_2, B_{12}, C and E (Surjushe *et al.,* 2008). Magnesium lactate which prevents histidine decarboxylase formation is also found in *Aloe vera* so it can act as anti-pruritic agent because histidine decarboxylase is required for the formation of histamine. *Aloe vera* gel has 22 amino acids in which 8 are essential amino acids and body cannot synthesize these amino acids. Mucilage of *Aloe vera* has mono and poly saccharides such as mannose, glucose and acemannan which act as an immune stimulant against psoriasis vulgaris (Paulsen *et al.,* 2005). For the anti-inflammatory and analgesic effects salicylic acid is the bioactive component found in the plant. Gibberellins and Auxins hormones are also found which help in wound healing and repair of the tissues. Flavonoids (Hu *et al.,* 2003, Mishra *et al.,* 2011), saponins (Kumar *et al.,* 2007) are also present in *Aloe vera* which may show the CNS depressant activity.

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METHODOLOGY

Long-term dosing was carried out on albino mice weighing from 25 – 30 gm with equal sex distribution. All animals were randomly assigned into two groups, one group served as control, while other group served as treated group each containing ten animals.

Housing

Albino mice were maintained in 22 ± 1^{o}C room temperature with 12/12 hours light - dark cycle i.e. light on from 08.00 am to 08.00 p.m at the Department of Pharmacology, University of Karachi and had access to water and food *ad labitum.* They were housed two per cage under standard conditions and kept at least 1 week before start of dosing.

Dosing

The dosing for biogenic amines analysis was in the dose of 500 mg/70 kg daily for a period of 30 days orally. The control group received saline (0.9% NaCl) by the same route as the treated group according to the body weight of animal.

BEHAVIORAL STUDIES

Head Dip Test

For the Exploration and learning ability, the Head Dip Test was used (Kliethermes and Crabbe., 2006), consisted a wooden Board (35cm x 45cm x 45cm) with 10 holes evenly spaced (2.5cm diameter). Albino mice control and treated groups were placed in an Exploratory Box for Head dip for 10 minutes and count the number of head dips after the administration of *Aloe vera* at 7, 15 and 30 days interval.

Open Field Activity

For the Behavior and Spontaneous Locomotor activity, Open Field Test (Tamada *et al.,* 2010) was used, consisted a wooden Board (76cm length x 76cm width x 40cm height) with 25 squares of even in size and escaping was prevented by the surrounded walls (Tahira *et al*., 2009). Albino mice control and treated groups were placed in the central square of the Open Field apparatus separately for 10 minutes and count the number of squares crossed after the administration of *Aloe vera* at 7, 15 and 30 days interval.

Swimming – induced Depression

Behavioral activity for the assessment of depression in rodents (Drugan *et al.,* 2010), Swimming-induced Depression Test was used consisted of a acrylic glass cylinder (20cm in height, 6cm in diameters) filled with water (25±2^{o}C) at specific level (12cm high) and escaping was prevented by the surrounded walls. Albino mice control and treated groups were introduced in the cylinder separately and note the struggling time after the administration of *Aloe vera* at 7, 15 and 30 days interval.

Stationary Rod Test

For the Learning ability, the Stationary Rod Test (Kishioka *et al.,* 2009) was used consisted of stainless steel rods with the platforms, giving a brief training before start of experiment. Albino mice control and treated groups were placed in the centre of the rod and allowed to walk separately and note the time of crossing the rod to another platform before administration of drug and repeat the experiment after the administration of *Aloe vera* at 7, 15 and 30 days interval.

Cage Crossing Activity

For the locomotor activity, Cage Crossing Activity (Prut and Belzung., 2003) was used consisted a transparent cage (26cm x26cm x 26cm) and escaping was prevented by the surrounded walls. Albino mice control and treated groups were placed in the transparent cage separately for 10 minutes and count the number of crossing (Tahira *et al.,* 2006) after administration of *Aloe vera* at 7, 15 and 30 days interval.

Inclined Plane Test

For the Muscular activity and hind limb strength, Inclined plane test (Jennifer *et al*., 2003) was used consisted a 30^{o} inclined screen. Albino mice control and treated groups were

introduced in inclined screen individually and note the time to cross the screen after the administration of *Aloe vera* at 7, 15 and 30 days interval.

STATISTICAL ANALYSIS

All results were expressed as average value ± Standard Deviation. The significance of difference between averages was determined by Newman (1939) and Keuls (1952) Test. Whereas the data obtained from present study was analyzed for P-value <0.01 was considered significant and P-value <0.001 was considered highly significant, following the one way ANOVA.

RESULTS AND DISCUSSION

Figures 1, 2, 3, 4, 5 and 6 show the Statistical analysis at 07 days, 15 days and 30 days of dosing of *Aloe vera* and data analyzed by One Way ANOVA shows a significant effect of drug *Aloe vera*.

Effect on Head Dip Test

In Fig 1, Post-hoc analysis by Newman-Keuls test shows that animals at 30 days of dosing of *Aloe vera* showed highly significant decrease in no. of Head Dips, i.e. 19±5.13 in comparison to control animals group, i.e. 31±3.01.

Animals at 15 days of dosing of *Aloe vera* showed significant decrease in no. of Head Dips, in comparison to control animals group, i.e. 31±3.01.

Animals at 07 days of dosing of *Aloe vera* showed non-significant decrease in no. of Head Dips, i.e. 25±7.43 in comparison to control animals group, i.e. 31±3.01.

Results showed that the no. of Head Dip of *Aloe vera* group was reduced much significantly after 30 days as compared to 7 days of dosing.

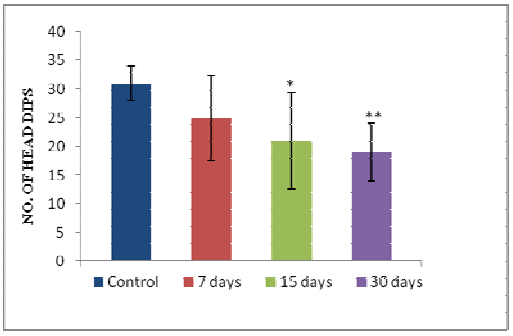

Figure 1. Effects of *Aloe vera* on Head dip Test in mice
n = 10
Average value ± St.Dev
Significant difference by Newman keuls test
*p < 0.01 as compared to control
**p< 0.001 as compared to control mice, following one way ANOVA

Effect on Open Field Test

In Fig. 2, Post-hoc analysis by Newman – Keuls test shows that animals at 30 days of dosing of *Aloe vera* showed significant decrease in no. of squares crossed, i.e. 110±32.93 in comparison to control animals group, i.e. 251±76.51.

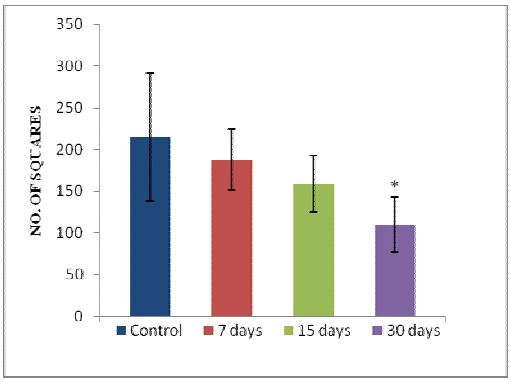

Figure 2. Effect of *Aloe vera* on open field Test in mice
n = 10
Average value ± St.Dev
Significant difference by Newman keuls test
*p<0.01 as compared to control mice, following one way ANOVA

Animals at 07 and 15 days of dosing of *Aloe vera* showed non-significant decrease in no. of Squares crossed, i.e. 188±36.45 and 159±33.71 respectively in comparison to control animals group, i.e. 251±76.51.

Results showed that the no. of Squares crossed by *Aloe vera* group after 30 days of dosing was reduced much significantly than after 7 and 15 days of dosing.

Effect on Swimming Induced Depression Test

In Fig. 3, Post-hoc analysis by Newman-Keuls test shows that animals after 30 days of dosing of *Aloe vera* showed significant decrease in Struggling time, i.e. 97±15.11 (sec) in comparison to control animals group, i.e. 136±22.21(sec).

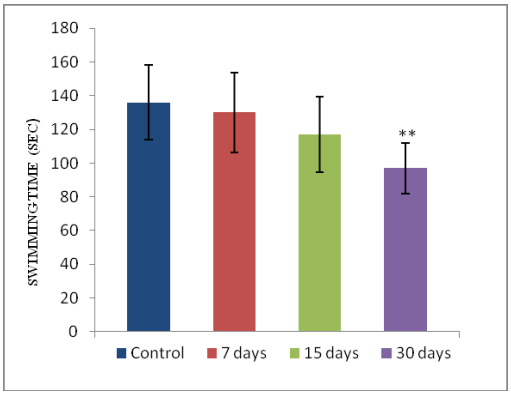

Figure 3. Effect of *Aloe vera* on Swimming induced depression Test
n = 10
Average value ± St.Dev
Significant difference by Newman keuls test
**p < 0.001 as compared to control mice, following one way ANOVA

Animals at 07 and 15 days of dosing of *Aloe vera* showed non - significant decrease in Struggling time, i.e. 130±23.61 and 117±22.53 (sec) respectively in comparison to control animals group, i.e. 136±22.21 (sec).

Results showed that the Struggling time (sec) of *Aloe vera* group after 30 days of dosing was reduced much significantly than after 7 and 15 days of dosing.

Effect on Stationary Test

In Fig 4, Post-hoc analysis by Newman-Keuls test shows that animals at 07, 15 and 30 days of dosing of *Aloe vera* showed highly significant increase in time taken to cross the rod, i.e. 18±5.92, 19±7.07 and 20±7.01 (sec) in comparison to control animals group, i.e. 8±2.05 (sec).

Results showed that the time taken to cross the rod (sec) by *Aloe vera* group after 7, 15 and 30 days was increased significantly.

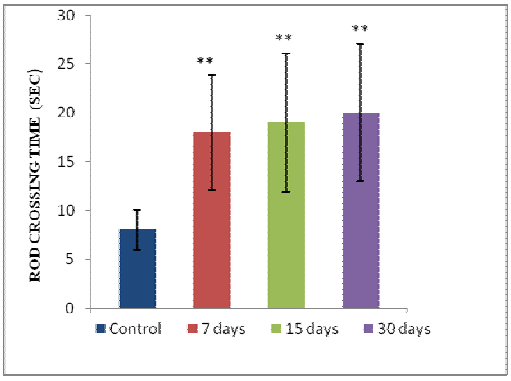

Figure 4. Effect of *Aloe vera* on stationary rod test
n = 10
Average value ± St.Dev
Significant difference by Newman keuls test
**p < 0.001 as compared to control mice, following one way ANOVA

Effect on Cage crossing activity

In Fig 5, Post-hoc analysis by Newman-Keuls test shows that animals at 30 days of dosing of *Aloe vera* showed highly significant decrease in no. of crossing of the Cage, i.e. 22±10.81 in comparison to control animals group, i.e. 66±33.35.

Animals at 07 and 15 days of dosing of *Aloe vera* showed non-significant decrease in no. of crossing of the Cage, i.e. 51±24.55 and 40±19.31 respectively in comparison to control animals group, i.e. 66±33.35.

Results showed that the no. of crossings of the Cage by *Aloe vera* group after 30 days of dosing was reduced much significantly than after 7 and 15 days of dosing.

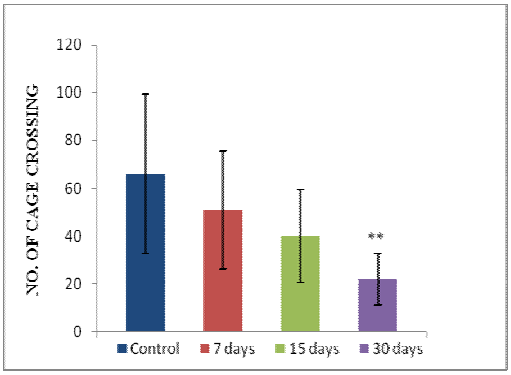

Figure 5. Effect of *Aloe vera* on cage crossing test
n = 10
Average value ± St.Dev
Significant difference by Newman keuls test
**p < 0.001 as compared to control mice, following one way ANOVA

Effect on Inclined screen test

in Fig 6, Post-hoc analysis by Newman-Keuls test shows that animals at 30 days of dosing of *Aloe vera* showed significant decrease in traction of the Inclined Plane (sec), i.e. 6±1.88 in comparison to control animals group, i.e. 11±4.47.

Animals at 07 and 15 days of dosing of *Aloe vera* showed non - significant decrease in traction of Inclined Plane (sec), i.e. 9±2.29 and 8±1.79 respectively in comparison to control animals group, i.e. 11±4.47.

Results showed that the traction of the Inclined Plane (sec) by *Aloe vera* group after 30 days was reduced much significantly than after 7 and 15 days of dosing.

DISCUSSION

Recently available drugs have side and toxic effects and new designed drugs also possess side effects as well as they are expensive. On the other hand herbal drugs are potent, effective, inexpensive and possess lesser side effects (Kumar *et al.*, 2010).

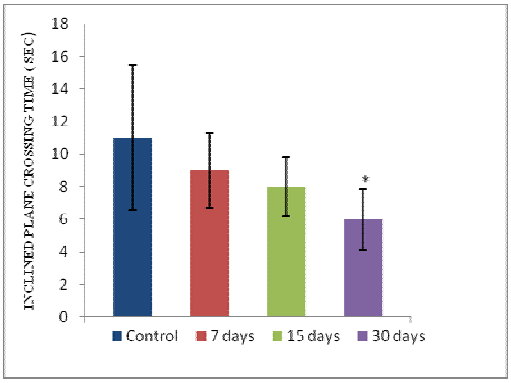

Figure 6. Effect of *Aloe vera* on inclined plane
n = 10
Average value ± St.Dev
Significant difference by Newman keuls test
*p < 0.01 as compared to control mice, following one way ANOVA

Exploratory and locomotor activities were measured in the Head dip test. The spontaneous activity of the animals was reduced after administration of drug. Decrease no. of head dips indicates the decrease in exploratory behavior and locomotion in animals. In the light of results it suggests that it has anxiolytic activity because of which the animal is not showing the exploratory activity. For the determination of the behavioral effects, locomotor, exploratory and anxiety – like behavior, open field test is used (Choleris., 2001). Open field test provides the measurement in term of frequency of squares crossed, used as measure for exploration and locomotion (Ajibade., 2011).

According to the Ardekani *et al* (2003), Davis *et al* (2003), Kubicki *et al* (2005), in schizophrenic condition brain ventricles are enlarged and white matter abnormalities are seen and in some other neuro imaging studies ,

antipsychotics have shown to provide the protection to white matter (Haiyun *et al.*, 2010). Antipsychotic both Typical and Atypical reduced the locomotor activity. In the present study also the open field activity in mice was decreased and it could be due to the reduced 5HT level, which was shown by *Aloe vera*.

Amygdala is a brain region involved in fear and anxiety responses and may be involved in several neurological disorders such as acute state of anxiety (Moya *et al.,* 2011) and 5HT is expressed in this brain region. 5HT enhances stress and shows an increased response to anxiety.

Psychological stress can be reduced by the tyrosine modulation or changes in dopamine and nor adrenaline concentrations may improve stress (Chen *et al.,* 2009). In current study *Aloe vera* could be involved in tyrosine modulation and can affect the level of dopamine. Due to this effect *Aloe* can reduce stress and produce anxiolytic response. This effect is observed by evaluating cage crossing and *Aloe* reduced the number of squares crossed.

In Forced swimming test, the swimming time of the animals was reduced and it could be due to the decreased muscle strength and also reduced due to anxiolytic response showing no stress to water.

Sakakibara *et al* (2005), reported that swimming stress is an essential factor of depression and during this 5HIAA/5HT ratio decreased significantly. In the long-term effects of *Aloe vera* the level of neurotransmitters detected by HPLC-EC, indicate that there was increase level of 5HIAA and 5 HT level was reduced changing the ratio.

For the muscular coordination and locomotor activity, stationary rod test was performed (Griffey *et al.,* 2006). Dopamine plays an important role in movement disorders such as Parkinson disease (Leng *et al*., 2004, Sedelis *et al*., 2000). In stationary rod activity animals were passive after the administration of *Aloe vera*, it could be due to anxiolytic effects and the result is in accordance to Niimia *et al* (2008). In recent study there is reduction in locomotor activity and muscular coordination resulting the passive behavior and not allowing the animals to reach the end point of the rod probably due to decreased level of 5HT. Viggiano *et al* (2003), reported that the striatum and cerebellum regions of brain are related to the muscular coordination and locomotor activity. In another study Galina and Pavlova (2001) reported that not only dopamine, 5HT is also involved in muscular coordination and locomotor control but the mechanism and effects of both are different in different species of animals as well as increase level of 5HT increase the locomotor but since current study shows reduction in locomotor activity it could be due to the decrease level of 5HT produced by *Aloe vera.*

In cage crossing test animals were passive as compared to the treated animal group. 5HT has an important role (Haleem *et al.,* 2002, Saima *et al.*, 2006). It could be due to decrease level of 5HT and it is also confirmed by Noreen *et al* (2005), that increased level of 5HT relieves depression.

Muscles relaxant activity of the animals was observed after administration of *Aloe vera* in 30^{o} inclined screen test. According to the Radhakrishnan *et al* (2001), the reduction in muscles strength is due to sedative action and anxiolytic activity observed due to decreased level of 5HT. The current study indicates decrease level of 5HT and increase in dopamine which could be responsible for the decreased muscles strength. The anxiolytic activity of *Aloe vera* needs further investigations so as confirm its use as anxiolytic agent.

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