Salvia hispanica (White chia): A new window for its antidepressant and memory boosting activity

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Abstract: To determine the effects of *Salvia hispanica* on activities related to memory, anxiety and depression. Albino rats as well as albino mice were utilized in the current study. Two groups of animals were made including 10 animals in each group. One was a control group and another was treated group. Neuropharmacological parameters were assessed using Light and Dark box test, Stationary rod activity, Water maze test, Open field activity and Home cage activity. The control group was maintained on water and treated group was fed with approximately 106 mg/kg extract of *Salvia hispanica* for 30 days. The observations were recorded on 1st day, 15th day and 30th day. The results of current study showed an increased time spent in the light box of Light and Dark box model, reduction in elapsed time utilized by animal to reach platform in Stationary rod and water maze model, reduced number of peripheral square and central square crosses in the open field and decreased number of cage crosses in the home cage activity. *Salvia hispanica* shows memory enhancement and also shows an antidepressant activity on chronic administration.

Keywords: Antioxidant, chronic disease, flavonoid, *Salvia hispanica*, stress.

INTRODUCTION

Salvia hispanica, also commonly known as "White Chia", belongs to specie of a flowering plant in the mint family known as Lamiaceae. This plant has a native origin of Central and Southern Mexico and Guatemala (United States Department of Agriculture, 2012). Seeds of *Salvia hispanica* contain abundant amounts of beneficial nutrients that enhance the life quality. Such nutrients include omega3 fatty acids and various antioxidants (Mohd Ali *et al*., 2012).

The constituents of *Salvia hispanica* contain various flavonoids. They also have polyphenol antioxidants such as kaempferol, chlorogenic acid, quercetin and caffeic acid (Ayerza *et al*., 2000; Ayerza *et al*., 2002a; Ayerza *et al*., 2002b). The antioxidants in *Salvia hispanica* are three times the amount of anti-oxidants as blueberries for equal volume. Apart from antioxidants, small chain omega-3 fatty acid alpha linoleic acid (ALA) and soluble and insoluble fibers are found in *Salvia hispanica.* Presence of all these chief and key components in *Salvia hispanica* provides a powerful defense against everyday stress and chronic disease processes (Martinez-Cruz *et al*, 2014; Ayerza, 2009).

Borneo *et al*. (2010) demonstrated that *Salvia hispanica* seeds have approximately 25% -35% of oil, especially in the form of poly-unsaturated fatty acids, approximately 22% of fiber and approximately 24% of protein (Ayerza and Coates, 2005; Capitani *et al*., 2012). After the oil extraction the residue remaining is known as chia meal which is a good source of proteins (19.0-23%), dietary fiber (~33.9-39.9%), and compounds that are rich in antioxidant activity (Marineli *et al*., 2014).

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MATERIALS AND METHODS

Water extract of plant

Salvia hispanica seeds was taken and soaked overnight in water then crushed or grinded next day morning. The dissolved water extract obtained was administered, to test animals.

Animals

Albino mice (24g), total 10 in number and albino rat (250g) total 10 in number were used for the experimental work. Diet and water was provided at libitum to the animals. (Hunter *et al*, 2005; Alexandra *et al*, 2016).The standard dose of the plant extract was 106mg/kg (1 tablespoon of *Salvia hispanica* =6.378g or 6378 mg that is 106 mg/kg adult dose). Following preliminary experiments, an optimum dose ranging from 2.5mg was arrived for mice and 21.2mg for rats. The extract was administered for 30 days.

Effects of Salvia hispanica on neuropharmacological activities in mice and rats

The effects of *Salvia hispanica* were assessed on a number of neuropharmacological activities using standard techniques.

Light and dark test

This apparatus comprises of a box having two compartments (20 × 20cm). The light and dark box is

divided into two compartments. One of the compartments is illuminated with light and one of them is kept dark. In the center of the illuminated compartment, the individual animal is placed and is facing one of dark place. Hence, the total number of entries in each space along with the time spent in light compartment as well as dark compartment is recorded for ten minutes respectively (Yogesh Chand *et al*., 2010).

Stationary rod activity

Prior to treatment, mice were given a short training period (2 or 3 trials). This pre-treatment training ensures that mice have ability to walk firmly across a horizontal type of steel rod (having diameter of approximately 5/8 and length of approximately 2ft) positioned 18 inches at height above the table surface. The mice were placed on the mid-point of the rod individually and were trained to walk forcefully towards a platform at either end of rod. The time taken to reach the plat form by the mice was determined in seconds (Rahila Najam, 2003).

Water maze test for rats

The water maze was developed by Richard Morris at University of St Andrews (Scotland) (Morris, 1981; Morris, Garrud Rawlins, Keefe, 1982). In water maze test, the rats were placed in a pool of water facing the pool-side to prevent any bias. The rats were required to escape from the water towards a hidden platform. By the use of specific spatial memory, the location of platform can normally be identified. The time taken by rats to reach platform was noted in seconds (Richard, 2008).

Open field

This method was described by Haleem *et al.* (1988). The activities were scored by counting the number of peripheral and central squares crossed by individual mouse during a 10 minute period (Rahila *et al.*, 2010).

Home cage activity

A specially designed apparatus as per international standards specifications is used for this activity. Specifically designed Perspex home cage (26 × 26 × 26 cm) with saw dust- covered floor were used to monitor cage activity. The experiment was performed in a separate room that was quiet. Mice treated with test were observed in their home cages 60 minutes post administration for 10 minutes to monitor the activity. During this time period number of cage crossing, climbing's, and grooming were counted (Haleem *et al*, 1988).

RESULTS

The effect of oral administration of *Salvia hispanica* for 30 days on different CNS parameters is shown in the following tables.

DISCUSSION

In the current study the plant *Salvia hispanica* was evaluated for its neuropharmacological effects. For evaluation of instinctive characteristics of rodents to dislike and avoid illuminated areas that are very bright and on the extemporaneous exploratory behavior of rodents that occurs in response to mild stressors such as novel environment and light, a test is performed which is termed as light and dark box (Bourin and Hascoet, 2003). The results of our study demonstrate that time spent in light box is increased. This result also witness the CNS antidepressant effect of plant upon chronic use. The polyphenol type of antioxidants such as quercetin, kaempferol, chlorogenic acid and caffeic acid are also the constituents of *Salvia hispanica* (Ayerza *et al*., 2000; Ayerza *et al*., 2002), that are contributing in this effect. Antidepressant and anxiolytic like activity is due to the presence of the phenolic and caffeic acid in the plant (Takeda *et al*., 2002; Pereira *et al*., 2005). Quercetin present in the plant can increase the Brain-derive neurotrophic factor (BDNF) levels in brain injury models (Yao *et al*., 2012).

In the Stationary Rod Activity it was observed by the results that following administration of *Salvia hispanica*, the animal crossed Stationary Rod in a lesser amount of time as compared to the control. This effect suggests that *Salvia hispanic*a enhances learning, memory and grip. This effect can be attributed to fact that a wide variety of brains enhancing nutrients are present in *Salvia hispanica* such as omega-3 fatty acids and other antioxidants (Mohd Ali *et al*., 2012). The polyphenol type of antioxidants such as quercetin, kaempferol, chlorogenic acid and caffeic acid are also the constituents of *Salvia hispanica* (Ayerza *et al*., 2000; Ayerza *et al*., 2002), that are contributing in this effect. Antioxidant effects and ability to improve the brain functions, memory enhancement, property of improving the senses, and delay in age-related cognitive decline are the foremost pharmacological beneficial effects for which Salvia plants are traditionally noted (Perry*et al*., 1999).

The effect on Water Maze activity also support the finding as time taken by the animal treated with the drug to reach the platform was decreased considerably in comparison to the control, so this can be attributed to the memory enhancing effects. Moreover, the ability to improve brain functions, improve memory, fasten and enhance senses, and prolong or delay age-related cognitive decline, as well as the antioxidant effects are the foremost pharmacological beneficial effects for which Salvia plants are noted traditionally (Perry *et al*., 1999).

In the Open field activity especially the peripheral square crosses were decreased significantly. We can say that *Salvia hispanica* possesses an antidepressant profile. This antidepressant property might have made the animal

Table 1: Effect of drug on light and dark activity

Time (in seconds) spent in illuminated box													
	Day 1				Day 15				Day 30				
Groups	Mean ± SD			t-test	Mean ± SD			t-test	Mean ± SD			t-test	
Control	137.7	±	1.7	***+++p<0.001	186.6	±	1.7	***+++p<0.001	234.2	±	1.4	***+++p<0.001	
Treated	303.1	±	2.0		410.5	±	1.5		509.1	±	2.2		

Values are mentioned as mean ± SD
***p<0.001: a significant difference from the control following t-test
Values are mentioned as mean ± SD. (n=10). Significant differences by Newman-Keuls test $^{+++}$p<0.001 in comparison to different days, following repeated measure ANOVA df (2, 64176.9).

Table 2: Effect of drug on stationary rod activity

Time (in seconds) required to reach platform												
	Day 1				Day 15				Day 30			
Groups	Mean ± SD			t-test	Mean ± SD			t-test	Mean ± SD			t-test
Control	13.9	±	1.3	$^{***+++}$p<0.001	11.0	±	1.2	***+++p<0.001	8.9	±	1.1	***+++p<0.001
Treated	7.8	±	1.3		3.8	±	1.1		2.6	±	0.8	

Values are mentioned as mean ± SD. (n=10). Significant differences by Newman-Keuls test $^{+++}$p<0.001 is in comparison to different days, following repeated measure ANOVA df (2, 59.57).

Table 3: Effect of drug on water maze activity (With blurring by powdered milk)

Time (in seconds) taken to reach platform												
	Day 1				Day 15				Day 30			
Groups	Mean ± SD			t-test	Mean ± SD			t-test	Mean ± SD			t-test
Control	25.0	±	1.5	***+++p<0.001	18.9	±	1.4	***+++p<0.001	9.9	±	1.1	***+++p<0.001
Treated	9.6	±	1.4		6.6	±	1.3		2.1	±	1.1	

Values are mentioned as mean ± SD. (n=10). Significant differences by Newman-Keuls test $^{+++}$p<0.001 is in comparison to different days, following repeated measure ANOVA df (2, 80.6).

Table 4: Effect of drug on open field activity

Table 4.1: Effect of Drug on Central Square Crosses

Total number of central square crosses / 10 minutes												
	Day 1				Day 15				Day 30			
Groups	Mean ± SD			t-test	Mean ± SD			t-test	Mean ± SD			t-test
Control	49.7	±	1.4	***+++p<0.001	41.1	±	1.2	***+++p<0.001	39.3	±	1.4	***+++p<0.001
Treated	18.0	±	1.1		12.1	±	1.4		4.7	±	1.1	

Values are mentioned as mean ± SD. (n=10). Significant differences by Newman-Keuls test $^{+++}$p<0.001 is in comparison to different days, following repeated measure ANOVA df (2, 278.85).

Table 4.2: Effect of Drug on Peripheral Square Crosses

Total number of peripheral square crosses / 10 minutes												
	Day 1				Day 15				Day 30			
Groups	Mean ± SD			t-test	Mean ± SD			t-test	Mean ± SD			t-test
Control	150.7	±	1.7	***+++p<0.001	139.9	±	1.5	***+++p<0.001	133.9	±	1.3	***+++p<0.001
Treated	57.0	±	1.5		69.6	±	1.8		97.3	±	1.3	

Values are mentioned as mean ± SD. (n=10). Significant differences by Newman-Keuls test $^{+++}$p<0.001 is in comparison to different days, following repeated measure ANOVA df (2, 1675).

Table 5: Effect of drug on home cage activity

Total number of cage crosses / 10 minutes												
	Day 1				Day 15				Day 30			
Groups	Mean ± SD			t-test	Mean ± SD			t-test	Mean ± SD			t-test
Control	29.9	±	1.4	***+++p<0.001	29.5	±	1.2	***+++p<0.001	26.6	±	1.1	***+++p<0.001
Treated	27.3	±	1.3		17.0	±	1.4		6.0	±	1.2	

Values are mentioned as mean ± SD. (n=10). Significant differences by Newman-Keuls test $^{+++}p<0.001$ is in comparison to different days, following repeated measure ANOVA df (2, 636.90).

comfortable and therefore, resulting in decrease exploration of open field. Moreover, in the model of the open field, the present study demonstrates that on chronic dosing also, the number of central square crosses is decreased as compared to the control.

In the Home Cage Activity the number of cage crosses was decreased significantly as compared to control on chronic dosing. Decrease in the number of cage crosses depicts decrease anxiety in the animal. Hence, *Salvia hispanica* provides a strong defense against day to day stress and chronic disease and able to cope life's stresses strongly (Martinez-Cruz *et al*, 2014; Ayerza, 2009).

CONCLUSION

Salvia hispanica is beneficial as an antidepressant agent, for cognitive and neurological conditions. It improves and enhances the cognitive skills, memory and brain functions. In the future prospects antioxidant studies of the seeds could be preceded and done.

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