# Ferulic Acids Attenuates Chronic Unpredictable Mild Stress Induced Depressive Behaviors in Animal Model of Depression and Memory Learning Deficits

*Muhammad Farhan[1*], Dua Saleem[1], Maria Arshad,[1] Ayesha Ahmed Soomro, Saher Asif[1], Shoaib Ahmed[2], Sadia Rehman[3], Anila Bibi[4] , Syeda Rabab Zehra[1]*

[1]Neurochemistry and Biochemical Neuropharmacology Research Unit, Department of Biochemistry, University of Karachi, Karachi, Pakistan
[2]Department of Biochemistry, Federal Urdu University for Arts, Science and Technology, Karachi, Pakistan
[3]Department of Biochemistry, Bahria University of Health Sciences, Karachi
[4] Department of Biochemistry, Jinnah Sindh Medical University, Karachi, Pakistan

## ABSTRACT

### OBJECTIVE

Previous studies have been demonstrated that high intimidate homeostatic and implies unfavorable mood changes, certain or intense feeling of dejection, oppressed. Unhappiness, despondency and down-hearted. The chronic stress leads to depression like symptoms. Due to the difference in steroidal level, women are more prone to stress than female. The objective of the study was to determine the impact of ferulic acid on behavioral and learning memory deficits in male rats induced by chronic unpredictable mild stress.

### METHODS

In this present study twenty four animals we were randomly divided into two equal groups (i) Unstressed and (ii) CUMS. Animals of both groups were further divided into two groups (i) Unstressed-Water (ii) Unstressed- Ferulic Acid (10 mg/kg/day), (iv) CUMS-Water (v) and CUMS-Ferulic Acid (10 mg/kg/day). Animals of the CUMS group were exposed to a schedule of chronic mild stress shown in table over a period of 14 days**,** while animals of unstressed groups remained in their home cages. Water or respective dose of ferulic acid (10 mg/kg/day) was given orally to animals each day 1 hr before exposing to daily schedule of CUMS as shown in table. Food intake and body weight changes were monitored on next day of the 1st, 7$^{th}$ and 14$^{th}$ stress. Locomotor activities were monitored in familiar environment (activity box) and novel environment (open field) on next day of 1$^{st}$, 7$^{th}$ and last stress.

### RESULTS

Results from this study revealed that Ferulic acid is a potent antidepressants it shows positive behavioral effects in all three tests.

**CONCLUSION**

Present study concluded that the flavonoids like ferulic acids and others can be used as potent antidepressant and in order to improved learning and memory ability in rat model of CUMS induced depressive like behavior models

Key Words: Chronic unpredictable mild stress, depression, learning and memory deficits, ferulic acids, exploratory activity

## 1. INTRODUCTION

Depression represents a major illness with both health and social consequences similar to chronic diseases such as diabetes, congestive heart failure and hypertension (Mo ¨ller HJ, Henkel V 2005). According to the World Health Organization, depression is an illness characterized by negative mood, decreased interest for pleasure, feelings of guilt, uneasy sleep, decreased appetite and energy, as well as poor brain concentration (Murray CJL, Lopez AD 1996). These feelings can be either acute or chronic, resulting in a reduced interest for life which can lead to extreme actions such as suicide. Depression is normally treated with various pharmaceutical agents or psychotherapeutic interventions or a combination of these. Current evidence shows that patients seeing a primary care provider are more likely to have a failed treatment than patients seeing a psychiatrist (Powers RH, Kniesner TJ et al., 2002) .This, however, does not suggest that pharmacological agents are unsuccessful in the treatment of depression. Indeed, a large number of studies show that different pharmacological treatments are successful in treating acute depressive episodes (.Mo ¨ller HJ, Henkel V 2005). In this light, a successful cooperation between primary and specialty mental health sectors is crucial, since most patients with depression first seek help in primary care (Klinkman MS 1997, Gilbody S et al., 2002 and Williams JW et al., 2002). Depression is also associated with significantly worse outcomes in a number of medical conditions (Chodosh J, Kado DM et al.,2007) and depression is an independent risk factor for early mortality (even after accounting for sociodemographic factors, suicide, and biological and behavioral risk factors, such as smoking, alcohol, and physical illness) (McCusker J et al.2007 Musselman DL et al.,1998 and Schulz R et al.,2000) Various

explanations for ‘‘accelerated aging’’ in depression have been proposed, such as the ‘‘glucocorticoid cascade’’ hypothesis (Sapolsky RM et al., 1986 and Sapolsky RM. Glucocorticoids 1999) and ‘‘allostatic load.’’(McEwen BS 2002). Discovering pathological processes in depression at the cellular level could help identify novel targets for treating depression and its comorbid medical conditions. Ferulic acid is a hydroxycinnamic acid, an organic compound. It is an abundant phenolic phytochemical found in plant cell walls, covalently bonded as side chains to molecules such as arabinoxylans. As a component of lignin, ferulic acid is a precursor in the manufacture of other aromatic compounds. The name is derived from the genus *Ferula*, referring to the giant fennel (*Ferulacommunis*). Ferulic acid is found in a number of vegetable sources, and occurs in particularly high concentrations in popcorn and bamboo shoots. It is a major metabolite of chlorogenic acids in humans along with caffeic and isoferulic acid, and is absorbed in the small intestine, whereas other metabolites such as dihydroferulic acid, feruloylglycine and dihydroferulic acid sulfate are produced from chlorogenic acid in the large intestine by the action of gut flora. In recent years, Chinese traditional medicine has begun to focus more on the treatment of depression. Ferulic acid (FA) (4-hydroxy-3-methoxycinnamic acid), is a phenolic acid which is present in many plants such as *Ferulateterrima* Kar. Et Kir., *Angelica sinensis*, *Cimicifuga foetida* L., and *Ligusticum chuanxiong* Hort. It has a variety of biological effects including anti-inflammatory, anti-epileptogenic, anticancer and antioxidant activities. In particular, a large number of animal experiments also show that FA can reverse memory loss in mice caused by inflammation, elevate the carbonyl protein level and reduce nerve cell injury. In our previous studies, we focused on the negative effect of PS on the offspring and the specific mechanism, including the impaired GR and increased HPA axis reactivity. Taken together, these studies suggest that FA improves the depression induced by stress, but the effect and underlying mechanisms remain unclear. Therefore, these findings compelled us to explore whether FA had an effect on improving depression induced by PS in offspring. Prenatal stress (PS) can increase the risk of nervous, endocrine and metabolic diseases, and immune dysfunction. Ferulic acid (FA) is a dietary phenolic acid that has pharmacological properties, including potent anti-inflammatory action. Prenatal stress (PS), which refers to stress during pregnancy, has been reported to exert a wide variety of negative emotional and behavioral effects on both human and animal offspring,

including depression, anxiety, attention deficit hyperactivity disorder, and especially learning and memory deficits (Rice, F.I.; Thapar et al., 2007 and Kessler RC 2003).

## 2. METHODS AND MATERIALS

### 2.1 ANIMAL

Locally bred male (180-200 g) albino- Wister rats purchased from Dow University of Health and Sciences (DUHS), Karachi, Pakistan were housed individually under 12- hr light and dark cycle and controlled room temperature (25 ± 2ºC) with free access to cubes of standard rodent diet and water, for a period of three days before experimentation.

### 2.2 EXPERIMENTAL PROTOCOL:

Twenty four animals were randomly divided into two equal groups (i) Unstressed and (ii) CUMS. Animals of both groups were further divided into two groups (i) Unstressed-Water (ii) Unstressed-Ferulic Acid (10 mg/kg/day), (iv) CUMS-Water (v) and CUMS-Ferulic Acid (10 mg/kg/day).Animals of the CUMS group were exposed to a schedule of chronic mild stress shown below over a period of 14 days **(Table 2.1)** while animals of unstressed groups remained in their home cages. Water or respective dose of ferulic acid (10 mg/kg/day) was given orally to animals each day 1 hr before\ exposing to daily schedule of CUMS (Table 2.1). Food intake and body weight changes were monitored on next day of the 1st, $7^{th}$ and $14^{th}$ stress. Locomotor activities were monitored in familiar environment (activity box) and novel environment (open field) on next day of $1^{st}$, $7^{th}$ and last stress.

### 2.2 BEHAVIORAL ASSESSMENTS

### 1. FOOD INTAKE:

24-h food intake or weekly food intake as required in a particular experiment were monitored. A weighed amount of food was placed in the hooper in the cage of each animal. Intake was monitored by weighing the food left in the hooper of the cage after the required time.

### 2. BODY WEIGHT (GROWTH RATE):

Body weight changes were monitored to find out the effect of treatments in respective chapters. The animals were weight daily or weekly as required by the respective experiment. Daily or

weekly growth rate changes were calculated as percentage of starting day weight (experiment day body weight/starting day body weight) X 100.

**Table: 2.1 CHRONIC UNPREDICTABLE MILD STRESS (CUMS) SCHEDULE:**

| S.# | Day | CUMS | Time |
|---|---|---|---|
| **1.** | **Day 1** | Exposed to 4°C for 50 minutes | 11:00 am |
| **2.** | **Day 2** | 60 min cage agitation (60 rpm) | 11:00 am |
| **3.** | **Day 3** | 60 min restrained stress (wire grid) | 11:00 am |
| **4.** | **Day 4** | 12 hrs water deprivation | 11:00 am to 11:00 pm |
| **5.** | **Day 5** | 3 hrs light off day time | 11:00 am to 02:00 pm |
| **6.** | **Day 6** | 60 min Noise Stress | 11:00 am |
| **7.** | **Day 7** | 60 min restraint stress(tube) | 11:00 am |
| **8.** | **Day 8** | Exposed to 4°C for 50 minutes | 11:00 am |
| **9.** | **Day 9** | 60 min cage agitation (60 rpm) | 11:00 am |
| **10.** | **Day 10** | 60 min restrained stress (wire grid) | 11:00 am |
| **11.** | **Day 11** | 12 hrs water deprivation | 11:00 am to 11:00 pm |
| **12.** | **Day 12** | 3 hrs light off day time | 11:00 am to 02:00 pm |
| **13.** | **Day 13** | 60 min Noise Stress | 11:00 am |
| **14.** | **Day 14** | 60 min restraint stress (tube) | 11:00 am |

### 3. ACTIVITY CAGE TEST:

The assessment of locomotive activity in a familiar environment was done by activity cage test. The apparatus used in this study was a square perspex activity cage (26 x 26 x 26 cm) with a saw dust covered floor **(Fig. 2.2)**. Testing was done in a quiet room under weight light as described by Haleem et al., 2007a. Before monitoring the activity animal was placed in it for 15 min for the habituation. Number of crossing across the cage was monitored for 10 minutes.

### 4. OPEN FIELD ACTIVITY TEST:

The determination of exploratory locomotive activity in a novel environment as it may be altered by respective treatments was done by open field activity test. The test consists of measuring the activity of rats in an open novel space, from which escape is prevented by a surrounding wall (Walsh and Cummins., 1976; Haleem & Batool., 1996). The open filed apparatus used in this present investigation consisted of a square area 76 x 76 cm with opaque walls 42 cm high. The floor of apparatus was divided by lines into 25 equal squares **(Fig. 2.3).** To determine the activity a rat was placed in the center squarer of the open field. The exploratory activity (number of square crossed with all four paws) were scored for 5 minutes.

### 5. LIGHT DARK TRANSITION BOX TEST

Light-dark box transition is used as measure of anxiety (Shimada et al., 1995). The test was conducted in a locally made two compartment box. The compartments of equal size (26 x 26 x 26 cm), with an access (12 x 12 cm) between the compartments, differed in their sensory properties. Walls of one compartment were light (transparent) and other dark (black). A rat placed in this box is expected to pass more time in the light compartment. To determine the activity a rat was introduce in the middle of the light compartment of the box. Entries and time spent in the light compartment were monitored for a cut off time of 5 min**.** Entry into a compartment of the box is defined as the placement of all four paws in the compartment of the activity box (Bourin and Hascoet. 2003). Increased number of entries and time spent in light compartment are used as an indicator of reduced anxiety states (Imaizumi et al., 1994).

## 6. FORCE SWIN TEST

Forced swim test is used for the determination of antidepressant activity. The apparatus is consisting of water filled transparent glass container with diameter 12cm and 22 cm height. Each animal allowed swimming in the apparatus containing water with maintained (25± 2) temperature. Swimming (struggling) time and the immobility (helpless behavior) time were recorded for the determination of antidepressant activity.

### 2.3 Statistical analysis

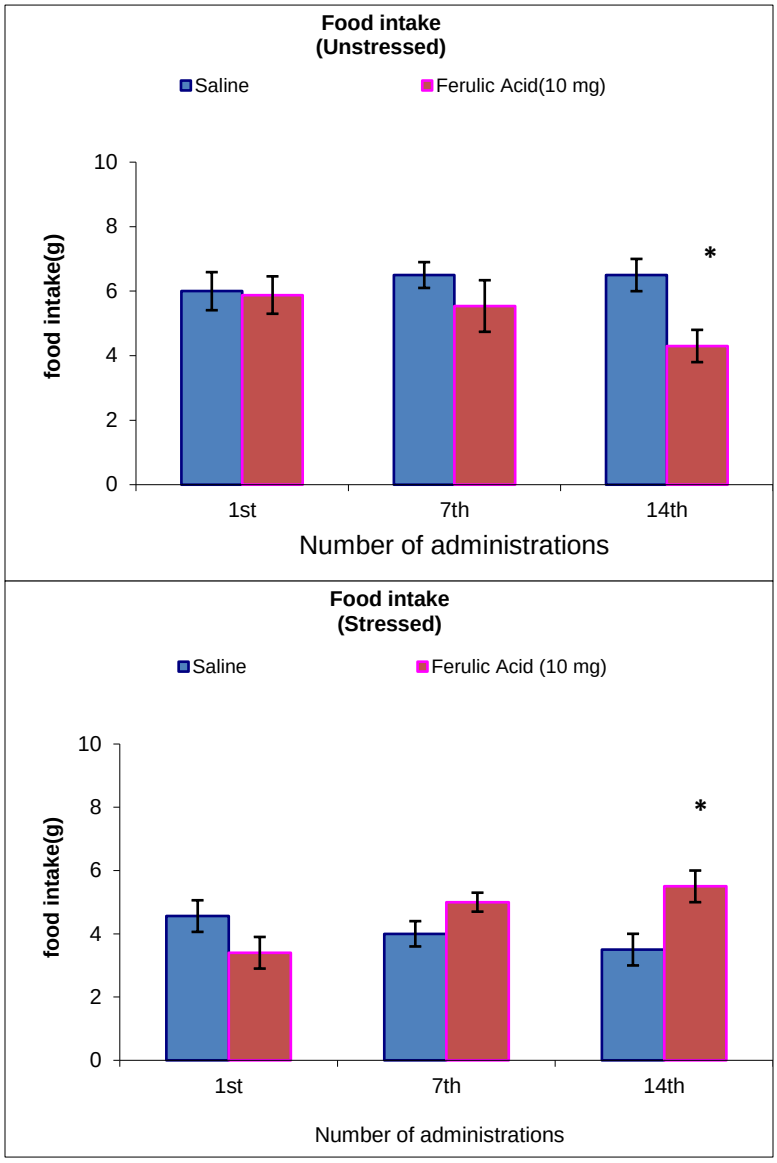
Values are means ± SD. Data were analyzed by three- way ANOVA (repeated measures design). Software used for the analysis was SPSS (version 17). Data on biochemical estimation were analyzed by two- way ANOVA. Post- hoc comparison was done by Newman-Keuls test. Values of $p<0.05$ were considered as significant.

## 3. RESULTS

### 3.1 EFFECTS OF FELURIC ACID ON CUMS–INDUCED BEHAVIORAL RESPONSES:

**Figure 3.1. Shows** effects of repeated ferulic acid administration on food intake of rats exposed to CUMS as monitored on next day of $1^{st}$, $7^{th}$ and $14^{th}$ stress. Data on food intake as analyzed by three- way ANOVA (repeated measures design) showed that effect of stress ($F=44.34$; df= 1, 32; $p<0.01$) was significant. Whereas, the effects of ferulic acid ($F=1.139$; df= 1, 32), repeated monitoring ($F=1.27$; df= 1, 32) and the interaction among the stress, ferulic acid and repeated monitoring ($F=1.87$; df= 1, 32) were not significant. Post-hoc analysis by Newman-Keuls test showed that exposure to CUMS decreased food intake in water treated animals and difference were significant after $14^{th}$ day of stress. Ferulic acid administration for $14^{th}$ days at dose 10 mg/kg decreased food intake in unstressed animals but increase was found in stressed group of animals.

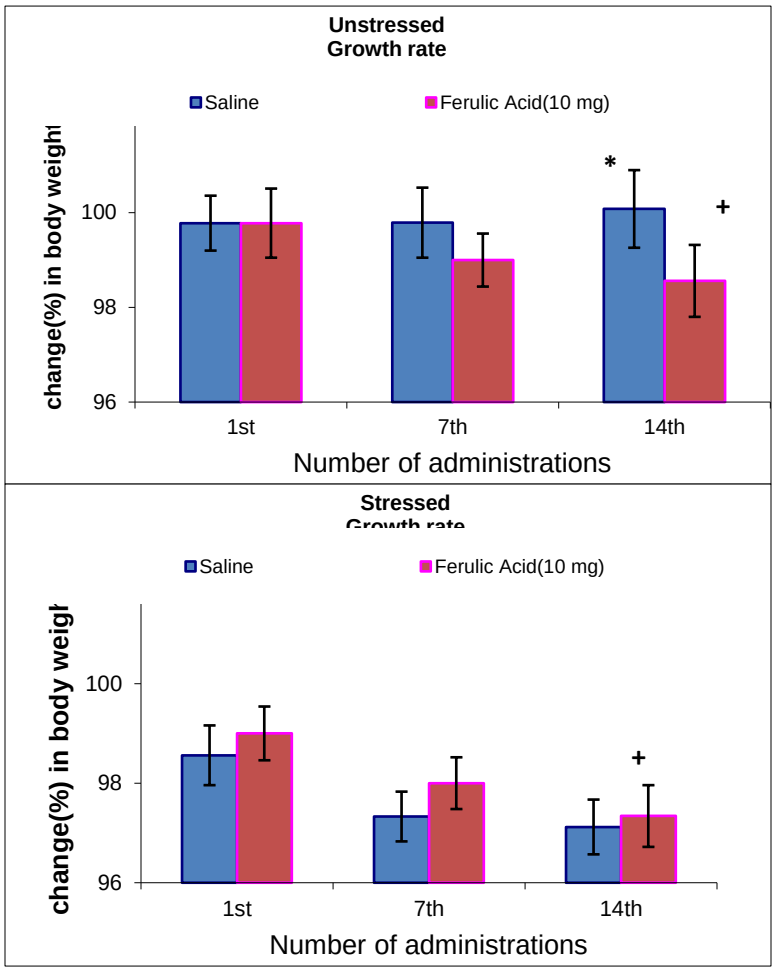
**Figure 3.1. Effects of administration of Ferulic acid (10 mg/kg/day) on food intake in unstressed and CUMS rats.**




Values are means ± SD (n=6) as monitored on next day of the administration. Significant differences by Newman-Keuls test:*p<0.05, **p<0.01 from respective unstressed animals; +p<0.05, ++p<0.01 from respective water treated animals. Following three-way ANOVA (repeated measure design).

**Figure 3.2. Shows** effects of repeated ferulic acid administration on body weight change of rats exposed to CUMS as monitored on next day of 1st, 7th and 14th stress. Data on growth rate as analyzed by three- way ANOVA (repeated measures design) showed that effect of stress ($F=92.51$; df= 1, 32; $p<0.01$) as well as the effect of ferulic acid ($F=41.46$; df= 1, 32; $p<0.01$) were significant. However, the effect of repeated monitoring ($F=1.32$; df= 1, 32) and the interaction among the stress, ferulic acid and repeated monitoring ($F=1.459$; df= 1, 32) were not significant. Post-hoc analysis by Newman-Keuls test showed administration of ferulic acid decreased growth rate in unstressed rats as well as in stressed rats as compared to saline administrated rats. Significant decrease was found after 14th day of administration ($p<0.05$). Administration of ferulic acid decrease growth rate in unstressed rats significantly ($p<0.05$) as compared to similarly administrated animals of 1st day administration.

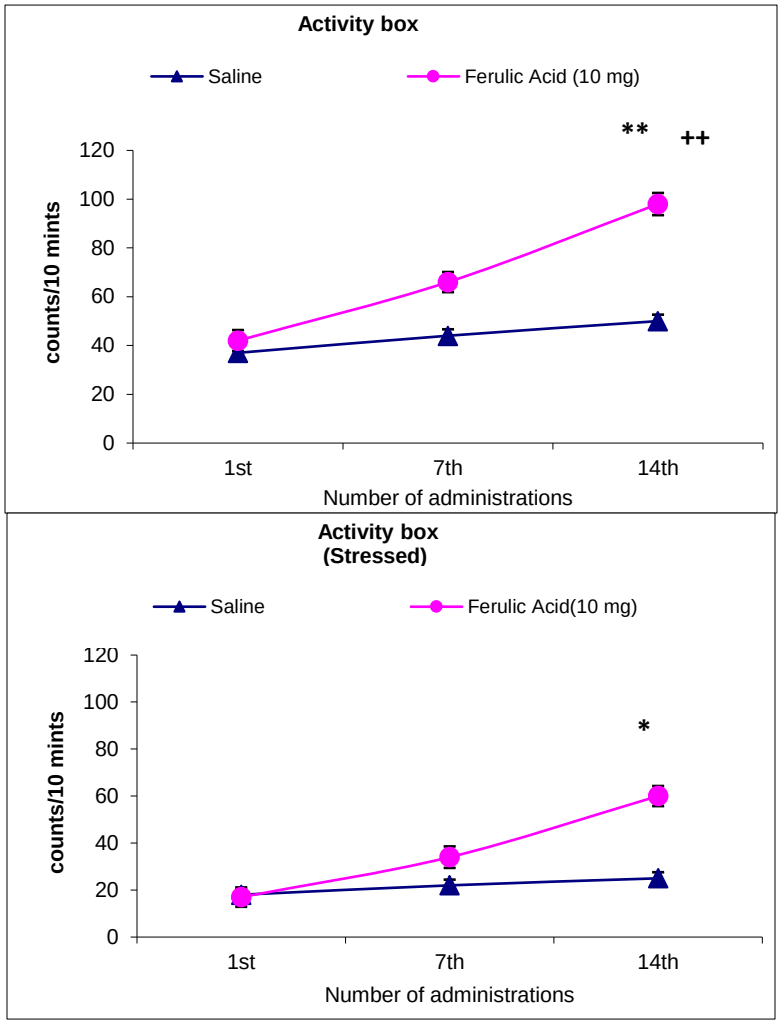
**Figure 3.2. Effects of administration of ferulic acid (10 m/kg/day) on growth rate in unstressed and CUMS rats.**




Values are means ± SD (n=6) as monitored on next day of the administration. Significant differences by Newman-Keuls test: *p<0.05, **p<0.01 from respective unstressed animals; +p<0.05, ++p<0.01 from respective water treated animals. Following three-way ANOVA (Repeated measures design)

**Figure 3.3 shows** effects of repeated ferulic acid administration (14 days) on activity in familiar environment (activity box) of rats exposed to CUMS as monitored on next day of 1$^{st}$, 7$^{th}$ and 14$^{th}$ stress. Data on number of cage crossing as analyzed by three- way ANOVA (repeated measures design) showed that effects of stress ($F=140.87$; $df= 1, 32$; $p<0.01$), ferulic acid ($F=74.12$; $df= 1, 32$; $p<0.01$), repeated monitoring ($F=48.45$; $df= 1, 32$; $p<0.01$) and the interaction among all the factors ($F=43.16$; $df= 1, 32$; $p<0.01$) were significant. Post-hoc analysis by Newman-Keuls test showed that administration of ferulic acid increase number of cage crossing in activity box of unstressed and stressed group animals as compared to saline administrated animals. Significant increase was found after 14$^{th}$ day of administration in unstressed ($p>0.01$) and stressed ($p<0.05$) animals. As compared to similarly administrated animals of 1$^{st}$ day administration of ferulic acid, activity in activity box was increase significantly ($p<0.01$) in unstressed animals on 14$^{th}$ day of administration.

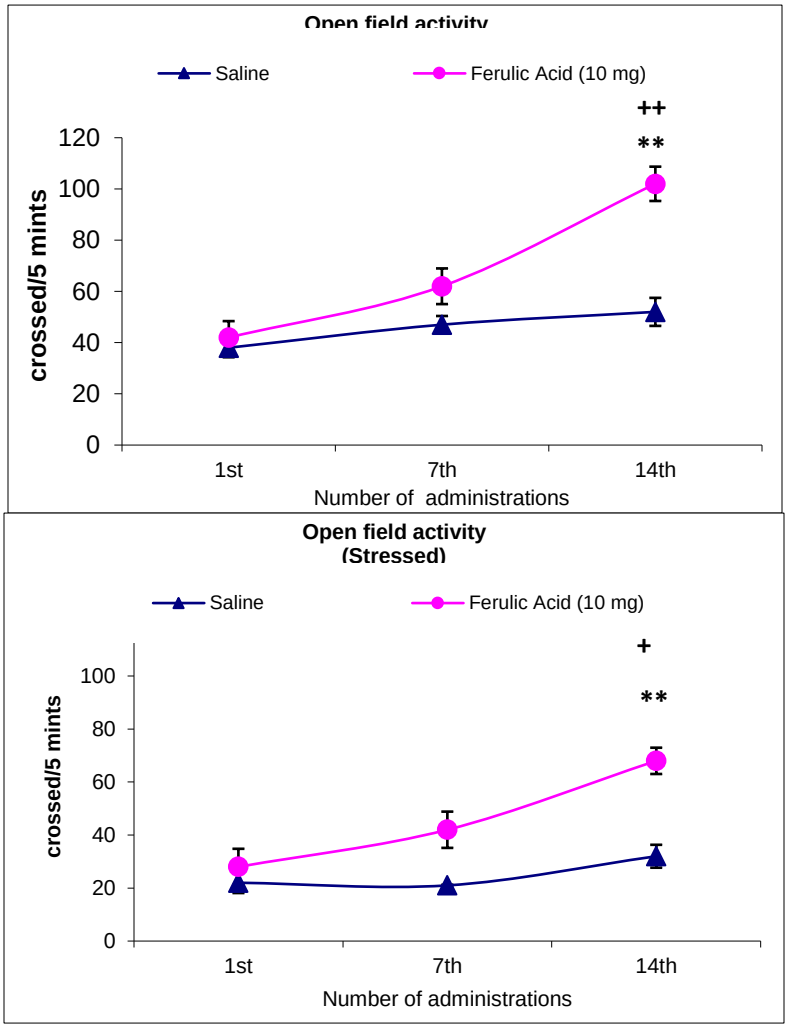
**Figure 3.3. Effects of administration of ferulic acid (10 mg/kg/day) on activity in familiar environment in unstressed and CUMS rats.**




Values are means ± SD (n=6) as monitored on next day of the administration. Significant differences by Newman-Keuls test: *p<0.05, **p<0.01 from respective unstressed animals; +p<0.05, ++p<0.01 from respective water treated unstressed or CUMS animals; # p<0.05, ## p<0.01 from respective day 1.0 mg/kg ferulic acid treated unstressed or CUMS animals following three-way ANOVA (repeated measure design)

**Figure 3.4 Shows** effects of repeated ferulic acid administration (14 days) on activity in novel environment (open field) of rats exposed to CUMS as monitored on next day of 1st, 7th and 14th stress. Data on number of square crossing as analyzed by three- way ANOVA (repeated measures design) showed that effects of repeated monitoring ($F=81.79$; $df= 1, 32$; $p<0.01$), ferulic acid ($F=62.15$; $df= 1, 32$; $p<0.01$) and stress ($F=102.14$; $df= 1, 32$; $p<0.01$) and interaction among CUMS, ferulic acid and repeated monitoring ($F=21.10$; $df= 1, 32$; $p<0.01$) were found significant. Post-hoc analysis by Newman-Keuls test showed that administration of ferulic acid increased activity in unstressed as well as in stressed group animals and values was significant after 14thday of administration at dose 10 mg/kg as compared to similarly treated saline administrated rats. Repeated administration of ferulic acid increase activity in unstressed ($p<0.01$) and stressed ($p<0.05$) group animals on 14th day of administration as compared to similarly administrated or treated animals of 1st day administration.

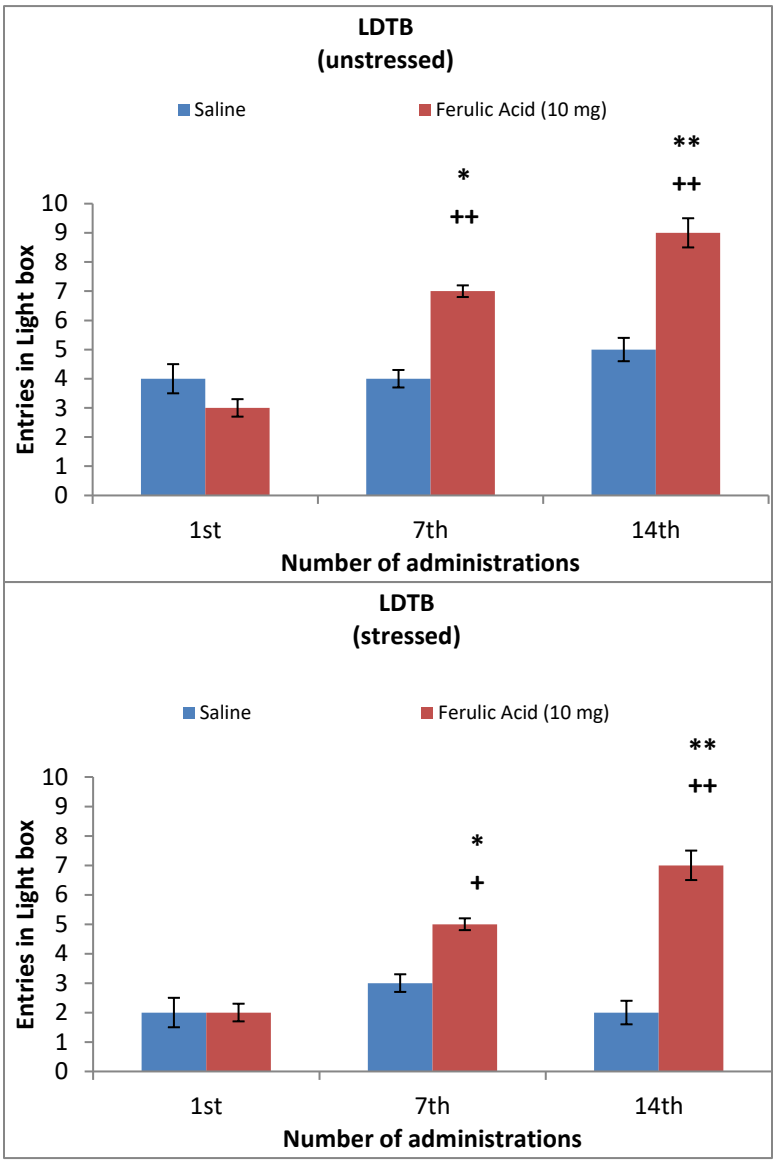
**Figure 3.4. Effects of administration of ferulic acid (10 mg/kg/day) on activity in open field in unstressed and CUMS rats.**




Values are means ± SD (n=6) as monitored on next day of the administration. Significant differences by Newman-Keuls test: *p<0.05, **p<0.01 from respective unstressed animals; +p<0.05, ++p<0.01 from respective water treated unstressed or CUMS animals; # p<0.01 from respective day 1.0 mg/kg ferulic acid treated unstressed or CUMS animals; following three-way ANOVA (repeated measure design).

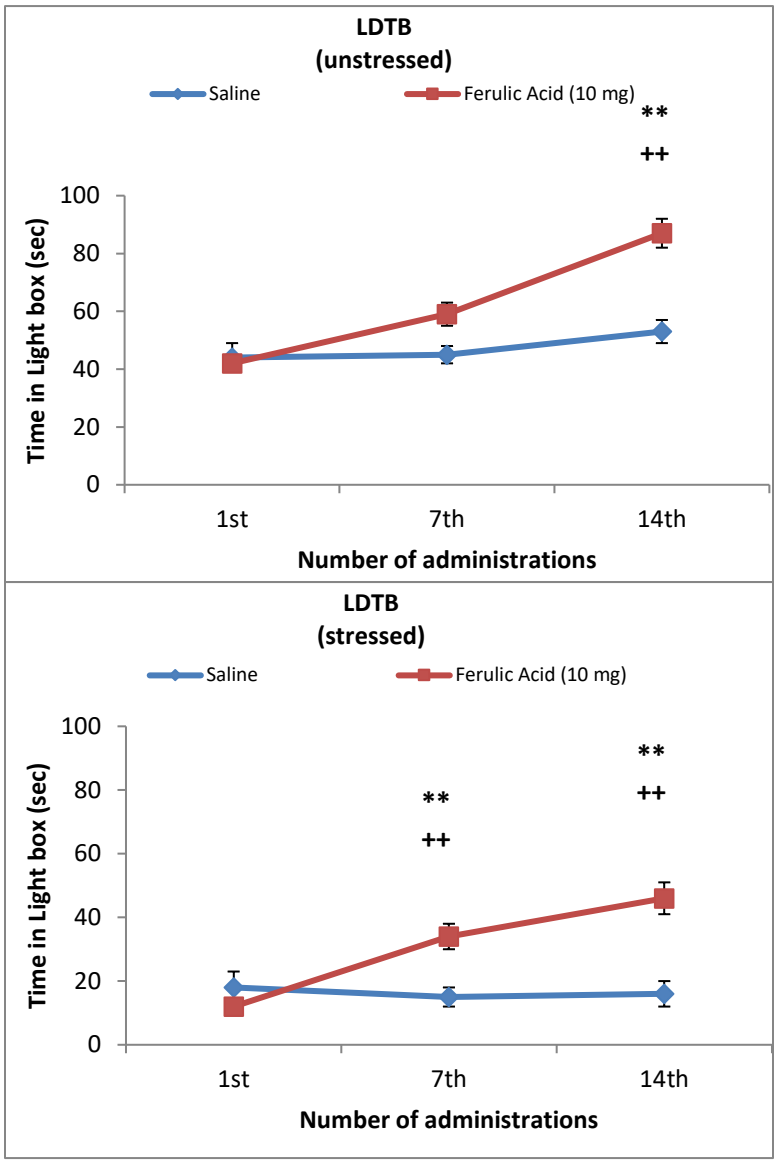
**Figure 3.5 Shows** effects of repeated ferulic acid administration (14 days) on activity in light dark transition box of rats exposed to CUMS as monitored on next day of 1st, 7th and 14th stress. Data on number of entries in light box as analyzed by three- way ANOVA (repeated measures design) showed that effects of drug ($F=43.61$; df= 1, 32; $p<0.01$), CUMS ($F=51.78$; df= 1, 32; $p<0.01$) and days ($F=24.94$; df= 1, 32; $p<0.01$) were found significant. However, the effects of interaction among CUMS, ferulic acid and days ($F=3.51$; df= 1, 32) were found no significant. Post-hoc analysis by Newman-Keuls test showed that administration of ferulic acid increased activity (number of entries in light box) in light dark transition box of unstressed as well as in stressed group animals and values was significant after 7th ($p<0.05$) and 14th ($p<0.01$) day of administration in unstressed as well as stressed animals compared to similarly treated saline administrated rats. Repeated administration of ferulic acid increase number of entries by rats in light box of unstressed and stressed group animals as compared to similarly administrated animals from 1st day of unstressed and stressed animals. Significant ($p<0.01$) increased was found after one week and 2nd week of administration in unstressed and after one week ($p<0.05$) and 2nd week ($p<0.01$) of stressed animals.

**Figure 3.5 Effects of administration of ferulic acid (10 mg/kg/day) on activity in LDTB of unstressed and CUMS rats.**




Values are means ± SD (n=6) as monitored on next day of the administration. Significant differences by Newman-Keuls test: *p<0.05, **p<0.01 from respective unstressed animals; +p<0.05, ++p<0.01 from respective water treated unstressed or CUMS animals; # p<0.01 from respective day 1.0 mg/kg ferulic acid treated unstressed or CUMS animals; following three-way ANOVA (repeated measure design).

**Figure 3.6 Effects of administration of ferulic acid (10 mg/kg/day) on activity in LDTB of unstressed and CUMS rats.**




Values are means ± SD (n=6) as monitored on next day of the administration. Significant differences by Newman-Keuls test: *p<0.05, **p<0.01 from respective unstressed animals; +p<0.05, ++p<0.01 from respective water treated unstressed or CUMS animals; # p<0.01 from respective day 1.0 mg/kg ferulic acid treated unstressed or CUMS animals; following three-way ANOVA (repeated measure design).

**Figure 3.6 Shows** effects of repeated ferulic acid administration (14 days) on activity in light dark transition box of rats exposed to CUMS as monitored on next day of $1^{st}$, $7^{th}$ and $14^{th}$ stress. Data on number of time spent in light box as analyzed by three- way ANOVA (repeated measures design) showed that effects of repeated monitoring ($F=68.29$; df= 1, 32; $p<0.01$), ferulic acid ($F=83.72$; df= 1, 32; $p<0.01$), stress ($F=44.69$; df= 1, 32; $p<0.01$) and the effects of interaction among all the factors ($F=62.54$; df= 1, 32;$p<0.01$) were found significant. Post-hoc analysis by Newman-Keuls test showed that administration of ferulic acid increased activity (time spent in light box) in light dark transition box of unstressed and stressed rats as compared to similarly treated unstressed or stressed saline administrated controls. Significant ($p<0.01$) increase was after $7^{th}$ and $14^{th}$ day of administration in stressed and in unstressed animals ($p<0.01$) after two weeks of administrations. As compared to single administration, the repeated administration of ferulic acid increase time spent in light box by rats of unstressed and stressed group animals as compared to similarly administrated animals from $1^{st}$ day of unstressed and stressed animals. Significant ($p<0.01$) increased was found after $7^{th}$ and $14^{th}$ day of administration in stressed animals and $14^{th}$ ($p<0.01$) of administrations in unstressed animals.

## 4. DISCUSSION

Stress is an acute feeling of despondency leading to chronic dejection of depression. In depression associated state an individual perceives to feel downhearted, hopeless, dispirited and oppressed despite of undefined reason chronic stress leads to depression. Depression has been likened to a state of ‘‘accelerated aging,’’ affecting the hippocampus and the cardiovascular (CV), cerebrovascular, neuroendocrine, metabolic, and immune systems, (McIntyre RS et al.,2007 and Bauer ME et al.,2008) and depressed individuals have a higher incidence of various diseases often associated with aging, such as Type II diabetes(McIntyre RS et al.,2007), metabolic syndrome (Evans DL, Charney DS et al.,2005), osteoporosis (McIntyre RS, Rasgon NL et al., 2009), CV disease (Brown ES, Varghese FP et al ., 2004) ,stroke, and pathological cognitive aging, including Alzheimer's disease and other dementias (Speck CE, Kukull WA et al.,1995) This current approach focuses on CUMS mediated depression associated model .CUMS has given to rats for 14 days by different methods including noise pollution ,cage agitation , low temperature etc. Twenty four animals were randomly divided into two equal groups (i) Unstressed and (ii) CUMS. Animals of both groups were further divided into two

groups (i) Unstressed-Water (ii) Unstressed- Ferulic Acid (10 mg/kg/day), (iv) CUMS-Water (v) and CUMS-Ferulic Acid (10 mg/kg/day). Animals of the CUMS group were exposed to a schedule of chronic mild stress shown below over a period of 14 days **given in table** while animals of unstressed groups remained in their home cages. Water or respective dose of ferulic acid (10 mg/kg/day) was given orally to animals each day 1 hr before exposing to daily schedule of CUMS (Table 2.1). Food intake and body weight changes were monitored on next day of the 1st, $7^{th}$ and $14^{th}$ stress. Locomotor activities were monitored in familiar environment (activity box) and novel environment (open field) on next day of $1^{st}$, $7^{th}$ and last stress. 24-h food intake or weekly food intake as required in a particular experiment were monitored. Body weight changes were monitored to find out the effect of treatments in respective chapters. The animals were weight daily or weekly as required by the respective experiment .The assessment of locomotive activity in a familiar environment was done by activity cage test. The apparatus used in this study was a square perspex activity cage (26 x 26 x 26 cm) with a saw dust covered floor .The determination of exploratory locomotive activity in a novel environment as it may be altered by respective treatments was done by open field activity test. In the end the result shows that ferulic acid acts as neuro proctectant against depression induced by CUMS because ferulic acid is natural antioxidant and naturally occurring compound and have no side effects In particular, a large number of animal experiments also show that FA can reverse memory loss in mice caused by inflammation, elevate the carbonyl protein level and reduce nerve cell injury. So in our present study it produced beneficial effects and increase activity of rats This study is useful in the determination of antidepressant effects of ferulic acid on UCUMS induced rats. One of the purposes of this research is to find the effectiveness and the safety for the treatment of Depression. This study helps us to identify the causes of depression because it is progressing worldwide and many people are getting more susceptible to the disorder. This study shows how Depression affects the people and how it is severe with time. This study suggests the effective effect of ferulic acid for the treatment of Depression because this disease has not much cure and cannot be treated without medications. The present study was planned to investigate the effect of ferulic acid as an antidepressant in comparison to fluoxetine because ferulic acid is a natural compound and has no side effects as fluoxetine have. Main focuses of the study to determine the effect of ferulic acid as an anti depressant and reduces the behavioral deficits and depression on rat's models which was induced by Unpredictable Chronic Mild Stress. In future we will regard

ferulic acid as neuroprotective and antidepressant. We will hope to reverse the depression mediated neuropsychiatric effect by administration of ferulic acid.

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