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**Research Paper**

# Effect of Curcumin in Chronic Stress Induced Anxiety in Wistar Rats

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***ABSTRACT***
***AIM:*** *The main objective of the study was to evaluate the anti anxiety activity of curcumin in chronic stress induced anxiety in winter rats.*
***Methods and Materials:*** *The investigation of antidepressant activity was carried out using Despair Swim Test (DST) and Tail Suspension Test (TST) and for anxiolytic activity Open Field Test (OFT) and Elevated Plus Maze Test (EPM)*
***Result:*** *The mean number of bright chamber entries in the Forced swim test controls is slightly increased in comparison to normal control group, it has also increased in diazepam treated groups whereas no increase in the mean number of bright chamber entries has been observed in the cur cumin treated groups at both the doses tested that is 60 mg/kg and 120 mg/kg. The mean number of rears has decreased in the Forced swim test control group whereas it has increased in the diazepam treated groups in comparison to normal control groups.The mean number of rears has decreased in the Forced swim test control group whereas it has increased in the diazepam treated groups in comparison to normal control groups.The mean time taken in onset of social interaction has increased in forced swim control test group and diazepam treated groups in comparison to normal control. The mean time taken in onset of social interaction has increased in the cur cumin treated group in comparison to normal control group at both the doses tested that is 60 mg/kg and 120 mg/kg.*
***Conclusion:*** *Chronic forced swimming as restrainer test model induced anxiogenic behaviour in rats in comparison to normal control group. The restrainer test model showed more anxiety in comparison to the normal control and forced swim test control group.*
***KEYWORDS:*** *Curcumin, antidepressant, diazepam, anxiolytic*

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## I. INTRODUCTION:

Anxiety is an strong emotion the disorders of which traces it's history almost equally with the evolution of humans [1]. Anxiety is an unpleasant state of inner turmoil often accompanied by nervous behaviour, somatic complaints and rumination [2]. Fear and anxiety are not synonymous, fear is a response to a real stimuli where as anxiety is an unknown fear to a self anticipated event [3]. People suffering from anxiety disorder try to avoid situations which can provoke anxiety or provoked anxiety earlier [4]. Anxiety disorder can become pathological and can precipitate or aggravate many neurological or cardiovascular and psychiatric disorders [1]. Anxiety is not a single disease but it consists of a group of disorders that includes Phobis, obsessive compulsive disorder, Post traumatic stress disorders and the list goes on [5].

Most common anxiety disorder which affect 50% of the population by the age of 11 years and 80% of the population by the age of 20 years across the globe is social phobia [6]. The prevalence rate for various anxiety disorder individually is 4.1 to 6.6% for generalised anxiety disorder, 2.3 to 2.7% for panic disorder, 2.3 to 2.6% for OCD, 2.6 to 13.3% for social phobia [6,7]. Various lifetime anxiety disorder have a female to male ratio of 3:2 [8]. Different anxiety disorders like Generalized Anxiety Disorder, Phobia, Obsession, Hysteria have a prevalence rate varying between 4 to 6% in Indian [1].

Use of plant and its products for the development of drugs are since time immemorial. According to an estimate 60% of the drugs for the treatment of cancers as well as infectious diseases in market at present are of plant origin. The on going hunt for the development of newer drugs with high efficacy and potency and decreased adverse effects has found plant source as a plethora of opportunities [9].

Curcumin, a principal curcuminoid of turmeric is a diarylheptanoid and a member of ginger family. Desmethoxycurcumin and bis-desmethoxycurcumin are two other turmeric's curcuminoids. Curcumin exists in two forms kept form and enrol form out of which it is the enrol form which is more stable energetically and remains in solid phase [10]. The bioavailability of cur cumin as it was observed in phase one clinical trial was poor. One factor which might be responsible for its low bioavailability is its poor absorption in water [11]. To find out the effect of cur cumin on various diseases such as multiple myeloma, pancreatic cancer, myelodysplastic syndrome, colon cancer, psoriasis, major depressive disorder and Alzheimer's disease is on its way [12].

The main objective of the study was to evaluate the anti anxiety activity of curcumin in chronic stress induced anxiety in winter rats.

## II. MATERIALS AND METHODS:

**Study design:** This was one year experimental study in wistaria rats.

**Animals:** wistaria rats weighing 180 to 250 grams inbred in the institutional animal house were used for the study. Rats were housed in clean polypropylene cages, three rats were kept in each cage, in a controlled environment (22º to 24º C) with a 12 hour light and dark cycle with standard chow contenting fat 4.15%, protein 22.15%, carbohydrates 4% (suppled by amruth laboratory manufactured by Pranav Agro Industries Ltd. Sangli) and water ad libitum. The rates were allowed to acclimatise to these conditions for one week. Experiments were performed during the light phase of the cycle (10 am to 5 pm).

**Curcumin:**Curcumin suspension was made in 2% gum acacia for administration.

**Drug and chemicals:** For administrationdistilled water were used to dissolve Diazepam 1mg/kg.

**Forced Swim Model:** The rat were subjected to chronic stress by forced swim model [13]. The apparatus consists of a transparent white plastic tub thirty seven centimetres in hight and thirty centimetres in diameter. The tub was filled with tap water at room temperature upto a hight of twenty five centimetres and the rat was kept into the tub, the height of the water column was so kept to see that the tail of the rat should not touch the bottom of the tub, the hight of the water column was so kept to see that the tail of the rat should not touch the bottom of the tub. The stress was induced in the experimental lab which is well illuminated and well ventilated and the procedure was carried out in the first half of the day. As soon as the animal was kept in the tub the stop watch was switched on, the stress was induced for the span of fifteen minutes. The same procedure was repeated for each rat and every time a new rat was placed in the tub the tub was washed and filled with fresh tap water at room temperature.

**Restrainer Model:** The restrainer test box is a rectangular plastic box, having an opening at the one side of the box only. The length of the restrainer box was fifteen centimetres whereas the wide of the box was three centimetres. The restrainer box was having a lock from the opened side which can be adjusted with a screw and it contained a hole from which the tail of the rodent can brought out. The animal was made to enter into the restrainer box from the opened side and the screw was adjusted so that the animal cannot push it back and escape out. This procedure was repeated daily for fifteen minutes for ten days with each rat. Every time a new animal was placed in the restrainer box it was cleaned by washing it under running tap water [14,15].

**Elevated Plus maze (EPM):** Elevated plus-maze apparatus consists of 50×10×40 cmof two open armsand two50×10×40 cm long enclosed arms, with an open roof, arranged so that the two open arms are opposite to each other. A height of 50 cm was the elevation of height. For 4 weeks once daily p.o. the Curcuminwas administered. Facing one of the enclosed arms, the rat was placed in the center of the maze [16,17].

**Open field test (OFT):** For various parametersin a square open field arena (68×68×45 cm) movements of rats were observed. 60 minutes before test treatments were given orally. The rats were observed for 5 min in a dark, ventilated, sound-attenuating box and following variables were evaluated: Locomotion, number of rearings, number of field segments entered and number of fecal boluses.

**Study procedure:** All rats received standard pelleted diet. Drugs were administrated orally to all the groups. A total of fifty four rats were randomly assigned to nine groups of sis rats each. The feeding and assessment schedule was given as per table 1.

**Table 1:** Treatment schedule

| Groups | Treatments | Dose |
|---|---|---|
| 1 | Normal Control (NC) | 2% gum acacia |
| 2 | Forced Swim Test Control (FST) | 2% gum acacia |
| 3 | Restrainer test control (RT) | 2% gum acacia |
| 4 | FST F/W DIAZEPAM (FST+DIA) | 1 mg/kg, orally |
| 5 | RT F/W by Diazepam (RT+DIA) | 1 mg/kg, orally |
| 6 | FST + 60 mg/kg of Curcumin (FST+CUR 60) | 60 mg/kg orally |
| 7 | FST + 120 mg/kg OF CURCUMIN (FST+CUR-60) | 120 mg/kg orally |
| 8 | RT + 60 mg/kg OF CURCUMIN (RT+CUR-60) | 60 mg/kg, orally |
| 9 | RT + 120 mg/kg OF CURCUMIN (RT+CUR-120) | 120 mg/kg, orally |

Statistical analysis: Data were expressed as Mean ± SD and was analysed using one way ANOVA followed by Tuckey's post hoc test. A p value less than 0.05 will be considered statistically significant. Analysis of data was done using SPSS version 16.0.

## III. RESULTS:

The mean number of bright chamber entries in the Forced swim test controls is slightly increased in comparison to normal control group, it has also increased in diazepam treated groups whereas no increase in the mean number of bright chamber entries has been observed in the cur cumin treated groups at both the doses tested that is 60 mg/kg and 120 mg/kg.

The mean number of bright chamber entries in Restrainer test control group has decreased in comparison to normal control group, whereas it has increased in the diazepam treated groups. The mean number of bright chamber entry in cur cumin treated groups has not increased at both the doses of cur cumin tested.

**Table 2:** Bright and dark arena test

| **Groups** | **Number of Bright Chamber entry** | **Time Spent in Bright Chamber** | **Number of Rears in Bright Chamber** | **Duration of Immobility (SEC)** |
|---|---|---|---|---|
| 1. Normal Control (NC) | 2.50 ± 0.548 | 36.50 ± 17.14 | 2.00 ± 1.265 | 55.50 ± 21.34 |
| 2. Forved swim test control (FST) | 2.83 ± 1.472 | 33.83 ± 16.13 | 2.50 ± 0.837 | 51.00 ± 47.84 |
| 3. Restrainer Test Control (RT) | 1.33 ± 0.516 | 6.67 ± 4.45 | 0.17 ± 0.408 | 142.17 ± 41.77 |
| 4. FST F/W By Diazepam | 4.50 ± 0.837 | 55.00 ± 9.716 | 4.50 ± 1.049 | 44.50 ± 35.04 |
| 5. RT F/W By Diazepam | 4.67 ± 0.816 | 81.83 ± 17.48 | 6.33 ± 1.506 | 37.00 ± 21.11 |

| | | | | |
|---|---|---|---|---|
| 6. FST + Curcumin 60 mg/kg | 1.67 ± 0.516 | 6.17 ± 3.189 | 0.33 ± 0.516 | 124.17 ± 50.44 |
| 7. FST + CURCUMIN 120 mg/kg | 2.50 ± 0.837 | 12.33 ± 4.803 | 1.00 ± 0.834 | 124.33 ± 14.081 |
| 8. RT + Curcumin 60 mg/kg | 1.17 ± 0.408 | 6.17 ± 2.317 | 0.50 ± 0.548 | 166.33 ± 13.307 |
| 9. RT + Curcumin 120 mg/kg | 1.33 ± 0.516 | 8.50 ± 6.221 | 1.00 ± 0.632 | 150.17 ± 23.284 |

The mean number of rears has decreased in the Forced swim test control group whereas it has increased in the diazepam treated groups in comparison to normal control groups. The mean number of rears has increased in cur cumin treated group in comparison to Forced swim test control group but has not increased in comparison to normal control at the dose of 60 mg/kg. The mean number of rears in curcumin treated groups has not increased in comparison to both forced swim test control group and normal control at 120 mg/kg.

**Table 3:** Open field test

| **Groups** | **Number of rears** | **Number of peripheral squares crossed** | **Number of central squares crossed** | **Time sent in central Squares** |
|---|---|---|---|---|
| 1. Normal Control (NC) | 10 ± 5.44 | 51.67 ± 15.02 | 13.33 ± 8.16 | 19.83 ± 12.007 |
| 2. Forved swim test control (FST) | 2.67 ± 0.816 | 22.00 ± 4.472 | 4.00 ± 1.414 | 4.00 ± 1.414 |
| 3. Restrainer Test Control (RT) | 2.67 ± 1.366 | 1.917 ± 5.419 | 3.17 ± 1.169 | 3.33 ± 1.033 |
| 4. FST F/W By Diazepam | 10.50 ± 1.049 | 101.17 ±12.952 | 51.17 ± 11.26 | 50.17 ± 19.21 |
| 5. RT F/W By Diazepam | 5.67 ± 0.816 | 90.67 ± 14.77 | 57.67 ± 12.83 | 52.17 ± 22.66 |
| 6. FST + Curcumin 60 mg/kg | 5.17 ± 5.492 | 27.50 ±12.26 | 7.33 ± 2.58 | 7.33 ± 2.58 |
| 7. FST + CURCUMIN 120 mg/kg | 2.00 ± 0.632 | 26.83 ± 6.735 | 8.50 ± 2.168 | 8.50 ±2.168 |
| 8. RT + Curcumin 60 mg/kg | 2.67 ± 1.211 | 33.00 ± 5.099 | 10.17 ± 1.722 | 10.17 ± 1.722 |
| 9. RT + Curcumin 120 mg/kg | 2.67 ± 1.211 | 34.50 ± 4.899 | 6.83 ± 1.941 | 6.83 ± 1.941 |

The mean number of open arm entries has decreased in forced swim test control group where as it has increased in diazepam treated group. The mean number of open arm entries has slightly decreased in the cur cumin treated groups in comparison to forced swim test groups and normal control group at both the dose tested that is 60 mg/kg and 120 mg/kg.

**Table 4:** Elevated Plus Maze Test

| **Groups** | **Number of rears** | **Number of peripheral squares crossed** | **Number of central squares crossed** | **Time sent in central Squares** |
|---|---|---|---|---|
| 1. Normal Control (NC) | 6.00 ± 1.265 | 4.50 ± 1.643 | 3.33 ± 1.966 | 157.00 ± 33.98 |
| 2. Forved swim test control (FST) | 3.33 ± 2.251 | 4.83 ± 2.137 | 0.00 ± 0.00 | 63.17 ± 48.01 |
| 3. Restrainer Test Control (RT) | 5.17 ± 4.119 | 5.50 ± 2.665 | 0.33 ± 0.516 | 97.17 ± 100.302 |
| 4. FST F/W By Diazepam | 10.67 ± 3.077 | 11.83 ± 2.563 | 9.83 ±1.472 | 196.33 ± 34.66 |
| 5. RT F/W By Diazepam | 10.50 ± 1.378 | 11.33 ± 1.633 | 10.67 ±2.160 | 170.33 ± 31.32 |

| | | | | |
|---|---|---|---|---|
| 6. FST + Curcumin 60 mg/kg | 2.33 ± 0.816 | 3.00 ± 1.095 | 0.33 ± 0.516 | 31.67 ± 16.24 |
| 7. FST + CURCUMIN 120 mg/kg | 1.83 ± 0.753 | 2.33 ± 0.616 | 0.50 ± 0548 | 10.00 ± 5.020 |
| 8. RT + Curcumin 60 mg/kg | 2.00 ± 0.632 | 2.33 ± 0.516 | 0.67 ± 0.516 | 12.67 ± 4.13 |
| 9. RT + Curcumin 120 mg/kg | 2.17 ± 0.753 | 2.17 ± 0.753 | 1.00 ± 0.632 | 14.00 ± 4.472 |

The mean number of closed arm entries has slightly increased in forced swim test control group and in diazepam treated group. The mean number of closed arm entries has decreased in the cur cumin treated groups in comparison to forced swim test groups and normal control group at both the doses tested that is 60 mg/kg and 120 mg/kg.

The mean time taken in onset of social interaction has increased in forced swim control test group and diazepam treated groups in comparison to normal control. The mean time taken in onset of social interaction has increased in the cur cumin treated group in comparison to normal control group at both the doses tested that is 60 mg/kg and 120 mg/kg.

**Table 5:** Social interaction test

| **Groups** | **Time taken in onset of social interaction** | **Time spent in social interaction** |
|---|---|---|
| 1. Normal Control (NC) | 24.83 ± 22.35 | 97.83 ± 51.44 |
| 2. Forved swim test control (FST) | 49.00 ± 13.78 | 89.50 ±10.84 |
| 3. Restrainer Test Control (RT) | 51.17 ± 19.68 | 62.83 ± 9.84 |
| 4. FST F/W By Diazepam | 30.00 ± 5.86 | 157.67 ± 13.86 |
| 5. RT F/W By Diazepam | 29.00 ± 6.22 | 161.83 ±12.82 |
| 6. FST + Curcumin 60 mg/kg | 46.83 ± 39.03 | 99.33 ± 29.42 |
| 7. FST + CURCUMIN 120 mg/kg | 42.67 ± 15.85 | 102.83 ± 11.75 |
| 8. RT + Curcumin 60 mg/kg | 65.33 ± 21.40 | 76.00 ± 20.42 |
| 9. RT + Curcumin 120 mg/kg | 70.00 ± 24.42 | 61.67 ± 19.79 |

## IV. DISCUSSION:

The bright chamber entries made by the rodents are a parameter to evaluate the level of anxiety in rats. If there is a decrease in the number of bright chamber entries it signifies that the rats are stressed or anxious, similarly if there is an increase in the number of bright chamber entries it shows a decrease in level of anxiety.

In this experiment it was observed that there was an insignificant increase in the mean number of bright chamber entries in the forced swim test control group, which shows that the rats were not stressed in comparison to normal control; they behaved as normal control rats. Whereas the diazepam treated groups showed a significant increase in the mean number of bright chamber entries. The cur cumin treated groups did not show any significant entries in the mean number of bright chamber entries at both the dose tested that is 60mg/kg and 120 mg/kg. This suggests that the diazepam treated group showed the anti anxiety effect whereas the cur cumin treated group did not show anti-anxiety effect.

In this experiment it was observed that there was an insignificant decrease in the mean time spent in the bright chamber in the forced swim test control group, which showed that the rats were stressed in comparison to normal control rats. Whereas the diazepam treated groups showed a significant increase in the mean time spent in bright chamber. The cur cumin treated groups showed a significant increase in the mean time spent in bright chamber at both the doses tested that is 60 mg/kg and 120 mg/kg. This suggests that the rats were stressed in the forced swim test control group, in the diazepam treated group as well as the cur cumin treated group the anti anxiety effect was observed.

In this experiment it was observed that there was an insignificant in the mean duration of immobility in the forced swim test control group, which shows that the rats were stressed in comparison to normal control group. Whereas the diazepam treated groups showed a insignificant decrease in the mean duration of immobility. The cur cumin treated group did not show any insignificant decrease in the mean duration of immobility number at both the doses tested that is 60 mg/kg and 120 mg/kg. This suggests that the rats were

stressed in the forced swim test control group. In the diazepam treated group the anti anxiety effect was observed. Anto anxity effect was not observed in cur cumin treated groups.

In this experiment it was observed that there was an insignificant increase in the mean duration go immobility in the forced swim test control group, which shows that the rats were stressed in comparison to normal control groups. Where as the diazepam treated group showed a insignificant decrease in the mean duration of immobility. The cur cumin treated groups did not show any significant decrease in the mean duration of immobility number at both the doses tested that is 60 mg/kg and 120 mg/kg. This suggest that the rats were stressed in the forced swim test control group. In the diazepam treated group the anti anxiety effect was observed. Anti-Anxiety effect was not observed in cur cumin treated groups.

The men time spent in central square has decreased in forced swim test control group where as it has significantly increased in diazepam treated group. The mean time spent in central square in the cur cumin treated groups has not increased significantly comparison to forced swim test control and normal control groups at both the doses tested that is 60 mg/kg and 120 mg/kg. This suggests that the rats were stressed in the forced swim test control group. In the diazepam treated group the anti anxiety effect was observed where as in the cur cumin treated group anti-anxiety effect was not observed.

The mean time taken in onset of social interaction by the rodents is a parameter to evaluate the level of anxiety in rats, if there is a increase in the mean time taken in onset of social interaction is signifies that the rats are stressed or anxious similarly if there is an decrease in the mean time taken in onset of social interaction it shows a decrease in level of anxiety.

## V. CONCLUSION:

Chronic forced swimming as restrainer test model induced anxiogenic behaviour in rats in comparison to normal control group. The restrainer test model showed more anxiety in comparison to the normal control and forced swim test control group. The diazepam treated group had shown anxiolytic effect in the both the groups that is forced swim test group and restrainer test group. The test compound curcumin did not show any anxiolytic effect at both the doses tested that is 60 mg/kg and 120 mg/kg.

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