Research Article

Study of effect of curcumin on heat stress-induced behavioral changes in rats

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ABSTRACT

Background: Moderate heat stress (HS) has been proven to cause significant behavioral changes in rats. Curcumin (CM) has been reported in various studies to reverse behavioral changes caused by various toxic agents such as lipopolysaccharide, oxaliplatin-cisplatin, and cadmium. **Objectives:** The aim of this study was to assess the efficacy of CM in reversing the behavioral changes induced by HS in male albino rats. **Materials and Methods:** CM (0.5 g/kg and 2.0 g/kg) was administered as oral suspension to male albino rats of Wistar strain for 5 consecutive days along with HS at 37 ± 0.5°C in a biological oxygen demand incubator (relative humidity 65–82%). Observations of behavioral changes were done during and after HS in control and experimental animals. **Results:** Depressive behavioral changes were noted in HS control animals. During HS, CM 0.5 animals showed excessive running while in CM 2.0 animals, running became moderate. After HS, observations showed that there is reversal of behavioral changes to a minimal level in CM 0.5 and to a moderate to normal level in CM 2.0 animals. **Conclusion:** The result of this study revealed that CM was effective in causing reversal of HS-induced depressive behavioral changes in rats but in a dose-dependent fashion.

KEY WORDS: Heat stress; Depression; Curcumin; Dose dependent

INTRODUCTION

Moderate heat stress (HS) has been reported to affect various organs of the body[1] as well as causes hepatic damage as assessed by biochemical, morphological, and morphometric parameters.[2] Apart from it, HS has been reported to cause behavioral changes in pigeons[3] and in rats during and after HS, leading to depression due to substantial rise in core body temperature.[1]

In a recent study, the protective effect of curcumin (CM) has been found against HS-induced liver damage.[4] CM is a yellow-orange powder and it is extracted from the turmeric plant (*Curcuma longa*). CM (diferuloylmethane) is the principal curcuminoid of the turmeric. Extensive researches done over the past century reported that CM had therapeutic role in arthritis, pulmonary, cardiovascular, Parkinson's, and Alzheimer's disease along with diabetes, atherosclerosis, hypercholesteremia, inflammatory bowel disease, ulcerative colitis, psoriasis, pancreatitis, and various GI cancers.[5]

Along with these protective effects, CM has also been reported to reverse the behavioral changes induced by lipopolysaccharide,[6] oxaliplatin-cisplatin,[7] and cadmium.[8]

However, the role of CM in reversal of HS-induced behavioral changes has not been studied so far. Therefore, the present study was undertaken to find out whether CM has protective effects against HS-induced behavioral changes in albino rats or not.

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Aims and Objectives

This study aims to assess the protective effect of CM against moderate HS-induced behavioral changes in albino rats.

MATERIALS AND METHODS

Animals

Inbred male Wistar strain albino rats weighing between 150 and 180 g were used following approval by the Animal Ethical Committee of HIMS, Dehradun. Rats were housed singly in polypropylene cages (43 cm × 29 cm × 15 cm) with a wire mesh top and a hygienic bed of rice husk under standard laboratory conditions at 25 ± 2°C (relative humidity 65–85%), with light and dark cycles of 10 and 14 h, respectively. The animals were given water *ad libitum* and fed freshly cooked food.[2] "Principles of laboratory animal care" (NIH Publication No. 82–23, revised 1985) guidelines[9] along with all applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

This article does not contain any studies with human participants performed by any of the authors.

Drug

CM was obtained as powder (CUR-500™, >95% pure; Indsaff, Batala, India) and stored at normal room temperature but away from direct sunlight and moisture.

Experimental Protocol

The animals were divided into four groups having six rats in each group. Each rat received equal volume of fresh distilled water (DW)/CM suspension in DW (1 ml/100 g) orally.[4] CM powder suspension was given daily at 10 am for 5 consecutive days, and the last dose was given on the 5th day 1 h before subjecting the rats to experiment. 1st and 2nd groups of rats were treated orally with DW while the Groups 3rd and 4th received CM powder suspension in DW in the low dose of 0.5 (chronic myeloid leukemia) and the high dose of 2.0 (Cochran–Mantel–Haenszel) g/kg. All animals were kept on fasting for 4 h before heat exposure. During the heat exposure period, only one animal was housed in each cage with liberty of movement and water *ad libitum* but no food. 1st group was not exposed to any HD (US, negative control) but kept at room temperature while the 2nd (positive control), 3rd (CM, 0.5 g/kg), and 4th (CM, 2.0 g/kg) groups were exposed to moderately high environmental temperatures (HS, 37 ± 0.5°C) in a biological oxygen demand incubator (relative humidity 65–82%) for 4 h daily (11:00 am–03:00 pm) for 5 consecutive days[4] while the 1st group was put in incubator at room temperature of 25 ± 2°C for the same period and condition. The selection of 5 days of HS method was done on the basis of our previous observation of HS-induced behavioral changes.[1]

Following heat exposure, the animals were restored to normal room temperature (25 ± 2°C) with water and normal food diet.

Behavioral Observations

Daily changes in behavior were noted in the US animals and all HS animals. For recording the behavioral changes, all the observations were noted in a checklist. In the checklist, all the observations were noted during and after heat exposure. During heat exposure, changes were noted in activity level, while after heat exposure, changes were noted in activity level, attitude/mood, spontaneous behavior, and provoked behavior. On the other hand, neurological changes, as tremor, convulsion, circling, paralysis, head tilt, and coma, were also sought to rule out any neurological damages, if any caused by moderate HS.[1]

Data Analysis

Data are expressed as mean ± standard error of mean of six animals in each group. The data were analyzed using both quantitative and qualitative techniques. The program "GraphPad Instat 3" was used for this analysis.

RESULTS

Behavioral observations are summarized in Table 1.

It is evident from behavioral observations that during and after HS, all the control and experimental animals felt restlessness and hypoactivity except CM 2.0 animals which showed moderate running and less time taken in becoming active again.

HS control and CM 0.5 animals showed disturbed sleep pattern, but CM 2.0 animals showed near normal pattern. CM 0.5 animals showed sluggish activities and movements without indulging in play while CM 2.0 animals indulged in play after some time.

CM 0.5 animals showed minimal changes in spontaneous and provoked behavior in comparison to 2.0 animals which showed moderate changes.

No neurological changes were observed in HS animals.

DISCUSSION

The HS control animals showed significant changes in activity levels during and after HS as well as changes in attitude/mood, spontaneous, and provoked behavior after HS period. These findings displayed that the exposure to HS

Table 1: Effect of moderate HS (4 h/day for 5 consecutive days at 37 ± 0.5°C) on behavior of albino rats

Parameters		US+DW	HS+DW	HS+CM 0.5	HS+CM 2.0
During HS	Activity level	Normal activity 1. No running in the cage 2. Normal drinking of water 3. No soaking of body with saliva and urine	Restlessness 1. Excessive running in the cage 2. Increased drinking of water 3. Soaked their body with saliva and urine	Restlessness 1. Excessive running in the cage 2. Increased drinking of water 3. Soaked their body with saliva and urine	Restlessness 1. Moderate running in the cage 2. Increased drinking of water 3. Soaked their body with saliva and urine
After heat stress	Activity level	Normal activity Animals neither huddled nor lethargic	Hypoactivity 1. Animals huddled, on placing them in cage, just after heat exposure 2. Lethargic for at least 3 hours.	Hypoactivity 1. Animals huddled, on placing them in cage, just after heat exposure 2. Lethargic for at least 3 hours	Hypoactive initially only 1. Animals huddled, on placing them in cage, just after heat exposure 2. Lethargic initially but after around 60 minutes starts moving sluggishly
	Attitude/ mood	Not depressed 1. Normal sleep pattern 2. No decreased activity 3. Indulged in play No weight loss No decreased food or water intake	Depressed 1. Disturbed sleep pattern 2. Decreased activity 3. Not indulged in play No weight loss No decreased food or water intake	Depressed 1. Disturbed sleep pattern 2. Sluggish activity 3. Moving but not indulged in play No weight loss No decreased food or water intake	Near normal 1. Near normal sleep pattern 2. Activity sluggish initially only 3. After 2–3 h indulged in play No weight loss No decreased food or water intake
	Spontaneous behavior*	Neither huddled nor isolated from cage mates and indulged in play	After heat exposure, initially huddled but later on isolation from cage mates and not indulged in play	After heat exposure, initially huddled but later on isolation from cage mates, moving freely but not indulged in play	After heat exposure, initially huddled, then isolated and moving but later on indulging in play but not swiftly
	Provoked behavior	Normal response	Minimal response	Minimal response	Moderate response

*These observations were made without disturbing the animal. HS: Heat stress, DW: Distilled water

could lead to behavioral changes akin to depression. CM 0.5 group showed minimal betterment in mood and spontaneous behavior, but in CM 2.0 group betterment was more marked up to moderate to normal level. Results of experimental group indicated protective effect of CM and showed that the CM was more protective in higher doses of 2.0 g/kg.

Behavioral changes observed in this study in HS control animals are similar to the results attained in previous study, and it was postulated that these changes are due to substantial rise in core body temperature.[1] HS has been reported to cause elevated level of serum cortisol along with other stress hormones,[10] and elevated levels of serum cortisol have been reported to be one of the most significant causes of these behavioral changes including depression.[11] Hence, it can be concluded from this discussion that HS caused rise in serum levels of stress hormone cortisone, leading to behavioral changes in rats.

In the present study, CM-treated animals showed betterment in behavioral changes. CM has also been reported to reverse the behavioral changes induced by lipopolysaccharide,[6] oxaliplatin-cisplatin,[7] and cadmium.[8] The most probable cause of this beneficial effect of CM treatment should be the decrease in levels of stress hormone cortisol along with reduction in levels of other stress busters as reported earlier.[11]

Strengths and Limitations

The strength of the present study is that it is dealing with important environmental aspect. This study has shown that the HS even of short duration may lead to behavioral changes and these changes can be reversed by CM. Second, not much has been done in this area and further studies can be done in this area. Study faced certain limitations; first, the sample size is small. Second, only male rats have been taken. Third, stress hormones have not been studied which can be observed in further studies.

CONCLUSION

The present study revealed that the moderate HS even of short duration led to behavioral changes akin to depression. CM has been found to have crucial role in this regard and was effective in a dose-dependent manner against the HS-induced behavioral changes in adult male Wistar albino rats.

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