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RESEARCH PAPER

Neurobehavioral study of green tea decoction against monosodium glutamate induced depression and anxiety in mice

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ABSTRACT

The aim of the study is to investigate the neurobehavioral effect of green tea decoction against monosodium glutamate induced depression and anxiety. The study was conducted on mice of either sex weighing 30-35 gm. The herbal tea decoction was prepared by boiling the powder for 10 minutes. Monosodium glutamate (MSG) at 4 mg/g was administered to the animals for two weeks. The behavioral studies were conducted using elevated plus maze, forced swim test and tail suspension method. The decoction of herbal tea was administered at three doses viz., 0.1 ml, 0.2 and 0.4 ml/kg for two weeks in the MSG induced depressed and anxiety animals. Tests for the identification of phytochemical constituents were done for the decoction. Results were analyzed by One-way Anova and $p<0.05$ was considered to indicate the significance. The data from the study indicated that MSG at 4 mg enhanced the duration of immobility and reduced the time spent in open arm suggesting depressive and anxiety states, respectively. The administration of decoction of green tea at higher doses (0.2 and 0.4 ml / 100 g) reversed significantly ($p<0.01$) the neurobehavioral changes induced by MSG. The phytochemical studies indicated that decoction of green tea contains alkaloid, glycosides, flavonoids, terpenoid, tannins and saponins. The analysis of the indicated that decoction of green tea at higher tested dose might possess antidepressant and anxiolytic effect against MSG-induced neurobehavioral changes. The effect of the decoction might be related to its phytochemical constituents.

Keywords: - Mono sodium glutamate, green tea, anxiety, depression and phytochemical constituents.

INTRODUCTION

Mono sodium glutamate (MSG) is a salt of sodium of glutamic acid. The glutamic acid is found in many of types of food especially that are rich in protein like tomatoes and cheese and meats. The MSG is used widely as additives and flavor enhancer for food in industry and restaurants [1].

MSG is a common ingredient in the processed foods. MSG considers as safe by FDA when

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taken in normal, but there are reports that suggest that MSG in large quantity causes deleterious effects on health. MSG is reported to produce chronic diseases such as diabetes, dyslipidemia and heart ailments [2].

The experimental injection of MSG in rodents has caused obesity leading to brain damage and other complications that are related to the metabolic syndrome [2]. Administration of MSG to experimental animals has elevated the fasting blood glucose and the markers for the dyslipidemia. Further, the studies done on the healthy subjects in China indicated an increased risk of overweight upon chronic exposure to dietary components containing MSG [2]. Other studies have indicated that MSG can induce neurobehavioral change like depression and anxiety in mice and rat [3].

Tea is a most common drink consumed by people around the world. There are two types viz., black and green tea. The green tea is made from leaves of *Camellia sinensis* that is unoxidized leaves. The regular consumption of green tea has been reported to possess many health benefits against diseases such as obesity, heart problem and depression [4].

Studies also indicated that green tea improves the health of human and animal by reducing weight and treat glucose level and play role for brain change and increase level of antioxidant [5]. Green tea with thiamin in high concentration is reported to help in reducing stress and anxiety and other neurobehavioral complications [4]. Studies also indicated that polyphenol present in green tea possess anxiolytic effect when it was tested in mice [6].

However, the role of green tea on the neurobehavioral changes induced by MSG is not widely studied in the literature.

METHODOLOGY

Drugs and solvent:

Green tea and mono sodium glutamate, ascorbic acid was procured from the authorized supplier of the college. The solvents and other reagents were procured from the college's store house and were of analytical grades.

Animals:

Swiss albino mice (both male and female) weighing 30-35 gm was used for the present study. Prior to the conduct of the study, approval from the Institutional Animal Ethics Committee was obtained (Approval ID # 2019-CP-03). The animals were maintained in the standard laboratory condition with 12 hr dark/bright environment. Animals were provided with pelleted food and water *ad-*

labitum. Randomly selected animals were grouped as follows:

Grouping of animals:

- ***Group-1***: Control (Normal saline)
- ***Group-2:*** Monosodium glutamate (MSG – 4 mg/g, oral for two weeks) [7]
- ***Group-3:*** Treatment-1: Low dose of green tea decoction (0.1 ml/100 gm, b.w, oral) [8]
- ***Group-4:*** Treatment-2: Medial dose of green tea decoction (0.2 ml/100 gm, b.w, oral)
- ***Group*-5**: Treatment-3: High dose of green tea decoction (0.4 ml/100 gm, b.w, oral)
- ***Group***-6: Standard group: Ascorbic acid (100 mg/kg, oral) [7]

Preparation of green tea decoction:

The commercially available green tea was used in this study. 20 gm of the green tea was boiled in 100 ml of water for 15 minutes. After cooling for10 minutes, the decoction was filtered using a cloth and was administered to the animals by oral route.

Induction of neurobehavioral change:

Monosodium glutamate (MSG) was administered by oral route daily for two weeks. The dose of [MSG – 4 mg/g, b.w] was mixed in the feeding bottle that contained the drinking water. The amount of MSG was determined depending on the total weight of animals in the cage and their daily water consumption.

Neurobehavioral tests:

A. Test for anxiety:

The experiment was done by using the elevated plus maze. The test was done as per the standard procedure described. The animals were kept in the open arm and the different parameters such as time spent in open arm, head dips from open arm and vertical climbing attempts from closed arm were recorded in 5 minutes. [9]

B. Test for depression:

i. Forced swim test –

The experiment was performed as per the procedures mentioned. The animals were allowed to forced swim in the water maintained at 25 ± 2^0C and the total duration immobility when the animal show no movements excepts that are need to maintain the floating state was recorded in 5 minutes. [10]

ii. Tail suspension test:

In this test, animals were suspended by tail as per the procedure described. The time of immobility when the animal does not show struggle and remains motionless passively are recorded in the duration in six minutes. [10]

Phytochemical constituents for decoction:

Phytochemical constituents were determined for the green tea decoction. Test for alkaloids, glycosides, tannins, flavonoids, terpenoids and saponins were performed and the changes in the color was observed and recorded for the presence or absence of the constituent. [11]

Statistics:

The data obtained from the study was statistically analyzed by one-way ANOVA and the significance of the comparison was considered if the *p* value was < 0.05.

RESULT

A. Effect of green tea decoction on the duration of immobility in forced swim and tail suspension tests.

The data from the antidepressant tests are summarized in Fig.-1. In the forced swim test, the administration of MSG (4 mg/g) to the mice significantly (p<0.001) increased the duration of immobility compared to control animals. The administration of green tea in dose 0.2 ml/100g decreased the duration immobility significantly (p<0.01) and at dose 0.4 ml/100 g showed further reduction (p<0.001) in immobility increased compared with the MSG treated mice. Administration of ascorbic acid at 100 mg/kg also showed significantly (p<0.001) reduction in the duration of immobility in the MSG-treated animals.

The observation from the tail suspension test indicated that administration of MSG at 4 mg/g significantly (p<0.001) increased the immobility compared to the control mice. The administration of green tea at the doses 0.2 m and 0.4 ml significantly (p<0.001) reduced the time of immobility compared to the MSG-treated animals. The lower dose of green tea (0.1 ml) did not produce significant change in the duration of immobility. Ascorbic acid used as a standard reduced (p<0.001) the time of immobility when compared with the challenge group.

B. Effect of green tea decoction on the monosodium glutamate (MSG) induced anxiety by using forced elevated plus maze in mice.

The data suggested that MSG administration significantly reduced the time spent in open arm (p<0.01), reduced number of head dips (p<0.05) and number of vertical climbing (p<0.05) compared to normal animals. The

green tea decoction at 0.1 mg / 100 g did not show significant variation in the tested parameters. Green tea at 0.2 ml produced significant (p<0.05) enhancement only in the number of head dips, while the higher dose (0.4 ml) of green tea exhibited significant (p<0.05) improvement in the duration of time spent in the open arm and also increased the number of head dip and vertical climbing compared to the challenge group. Ascorbic acid on the other hand produced a significant reversal (p<0.01) in the anxiogenic parameters induced by the MSG (Table#1).

Table-1: Effect of green tea decoction on the monosodium glutamate (MSG) induced anxiety by using forced elevated plus maze in mice.

Groups	Time spent in open arm	Number of head dips	Number of vertical climbing
Control	98.75 ± 8.60	20.75 ± 3.20	13.25 ± 2.77
MSG (4 mg/g)	59.78 ± 6.63**	9.66 ± 2.87*	5.29 ± 1.45*
MSG + Green tea (0.1ml/100g)	61.35 ± 6.04	12.56 ± 3.09	7.89 ± 1.28
MSG + Green tea (0.2ml/100g)	70.04 ± 5.59	18.71 ± 2.56 [a]	8.46 ± 1.73
MSG + Green tea (0.4ml/100g)	81.16 ± 6.09 [a]	18.92 ± 2.06 [a]	9.91 ± 1.64 [a]
MSG + Ascorbic acid (100 mg/kg)	86.29 ± 5.49 [a]	19.21 ± 1.96 [a]	11.59 ± 1.52[b]

Values are expressed as Mean ± SEM, N=6

Statistics: One-way Anova, *p<0.001 compared to control.

[a]p<0.01, [b]p<0.001 compared to MSG.

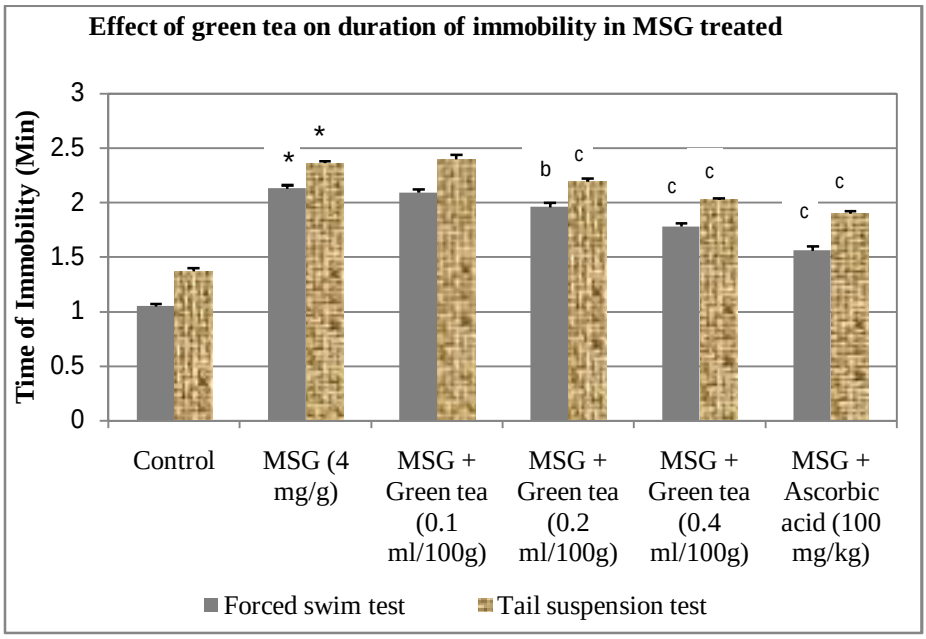
Table-2: Phytochemical analysis of the major constituents present in the green tea decoction.

Phytochemical test	Observation	Inference
Test for alkaloid	Yellow colored precipitates	Present
Test for glycosides (keller-killani test)	Violet-green ring	Present
Test for terpenoids (salkowski test)	Reddish bewon coloration	Present
Test for flavonoids	Yellow color clear on adding dil. HCL	Present
Test for tannins (extract +4 drop of FeCL3)	Blu-black coloration	Present
Test for saponins	Formation of emulsion	Present

C. Phytochemical analysis of the major constituents present in the green tea decoction.

The above table indicates the present of essential phytochemical constituents in the decoction of the green. Depending on the color

change after addition of the respective reagents, the observations were recorded to indicate the presence of alkaloid, glycosides, terpenoids, flavonoids, tannins and saponins (Table # 2).



Graph-1: Effect of green tea decoction on the duration of immobility in forced swim and tail suspension tests.

Values are expressed as Mean ± SEM, N=6
Statistics: One-way Anova, *p<0.001 compared to control, [a]p<0.01, [b]p<0.001 compared to MSG.

DISCUSSION

The results of this study indicated that administration of mono sodium glutamate (MSG) increased the duration of immobility in forced swim test and tail suspension test (Fig.-1). MSG treatment to mice also reduced the duration of time spent in the open arm and reduced the number of head dips from open arm and vertical climbing attempts from closed arm (Table#1). The observations suggest that MSG produced significant alterations in the neurobehavior to induce states of depression and anxiety in the animals.

Mono sodium glutamate is a common ingredient of processed food and in restaurants. The long term intake of this salt is reported to contribute in several complications of metabolism and neurophysiology. [1,3] The major neurophysiological complications include depression and anxiety. These states are characterized by isolation, lack of interest to work, agitation, palpitation, sweating etc. [12] Depression and anxiety are considered to

be major manifestations of neurobehavioral disease. The mechanism for the neurobehavior changes induced by MSG is related to the hippocampal GABA and 5-HT uptake pathways are reason in inducing the anxiolytic-like effect. [3.13]

Studies from the previous research indicate that the complications of dietary ingredients or environment pollutants can best prevented either by avoiding their exposure or by increasing the intake of those substances that can minimize the effects of these agents. Substances from the natural origin have been widely used for the treatment and prevention of various diseases and disorders. These agents are popular since *per se* they lack the adverse effects. [14]

The decoction of green tea when treated to the MSG-induced neurobehavioral modified animals it was observed that the higher doses of decoction (0.2 ml and 0.4 ml / 100 g) reduced significantly (p<0.01) the parameter of depression in both forced swim test as well in tail suspension method (Fig.#1). The test performed to evaluate the level of anxiety also suggested that decoction of green tea at higher tested doses reduced the anxiety parameters in the MSG-treated animals (Table # 1). These data suggested that decoction of green tea might possess the properties of antidepressant and anti-anxiety.

Earlier studies indicated that green tea administration has reduced the depression and anxiety in the experimental conditions. The mechanism has been suggested to be due to the presence of essential phytochemical constituents such as flavonoids, saponins, tannins etc. [5] In our study also we observed that the decoction of green tea contain the presence of essential constituents such as alkaloids, glycosides besides flavonoids, tannins and saponins (Table#2). We suggest that the phytochemical constituents present in the decoction might have reduced the noxious effects of MSG responsible for depression and anxiety.

One of the mechanism suggested is the antioxidant properties of these vital phytochemical to reduce the damaging effect of free radicals in the brain centers controlling the emotions [15] The reduction in the depression and anxiety due to antioxidant effect can be further substantiated from the observation as well from the previous studies on ascorbic acid [16] where it reduced the depression and anxiety parameters in the MSG-treated animals (Fig.#1 and Table#1).

CONCLUSION

The data from the present study indicated that MSG administration in the mice produced neurobehavioral changes characterized as depression and anxiety. Treatment of green tea decoction at higher doses (0.2 and 0.4 ml / 100g) reduced these changes and suggested that the decoction might possess the antidepressant and anxiolytic activities. The effect of the decoction of green tea can be related to the presence of essential phytochemical constituents.

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