Research Article

The Neuroprotective Effect of Curcumin Cumin Against Oxidative Stress- Induced by Acrylamide in Male Rats

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Abstract | Rats exposed to Acrylamide)ACR(displayed a neurotoxicity and alteration in behaviors. Curcumin (CUR) is useful in reducing behavioral flaws and restoring a normal body systems' function. The goal of the current study is to evaluate the how the brain effected oxidatively by Acrylamide exposure and the ability of Curcumin to ameliorate the neurotoxicity. For this investigation, thirty mature male albino rats be used, (10/group), the control group (CC), animals were intubated with distilled water for 40 days, Group G1, rats received Acrylamide 5 mg/kg B.W. every day for 40 days by gavage needle, and Group G2, in this group animals got Acrylamide 5 mg/kg B.W. and Curcumin 100 mg/kg B.W. for 40 days by gavage needle as well. At the zero and the end times of the experiment, blood samples were taken using the heart puncture technique after the subjects had been given an intramuscular injection of ketamine and xylazine to induce anesthesia. The findings revealed the exposure of Acrylamide to rats significantly reduced their tendency to gain weight, a marked rise in the concentration of malondialdehyde and decrease levels of Total antioxidant in blood serum and behavioral differences like Acrylamide greatly decreased the struggling and ascending time in the swimming test, dramatically lengthens the time needed to turn an animal's head 180 degrees during a negative geotaxis test and decreased locomotors activity in the Y maze test. Curcumin's anti-apoptotic, anti-inflammatory, and antioxidant properties have not been thoroughly examined in neurotoxicity given on by Acrylamide, nevertheless. We investigated whether Curcumin may protect against oxidative stress, apoptosis, and inflammation in neurons brought on by Acrylamide exposure. In conclusion acrylamide alters the neurobehaviors and oxidatively stressed animals .However Curcumin restored these parameters close to control values.

Keywords | Curcumin, oxidative stress, Acrylamide, Neurotoxicity, Behavioral, Male Rats, Biochemical indices, Antioxidants, herbal medicine

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INTRODUCTION

Acrylamide (ACR) is an important chemical, used in several commercial and scientific processes, such as gel electrophoresis, cosmetics production, and water purification (Kenwood et al., 2022). Smoke from cigarettes and meals high in carbs that have been cooked at high temperatures both contain high levels of Acrylamide (Bušová et al., 2022). It was believed that Acrylamide exposure only happened at work in industrial field, however, drinking polluted water, using cosmetics, and cigarette smoking all contributed to its exposure (Khudiar and Hussein, 2017). Additionally, the chemical building block Acrylamide, which is used to make polyacrylamide , may be modified to have nonionic, anionic, or cationic properties for certain applications (González et al., 2022). The neurotoxicity of

Acrylamide has been shown by both animal and human occupational exposure. Studies in a range of laboratory animal species, including rats, mice, guinea pigs, rabbits, and monkeys, have shown that repeated daily exposure to Acrylamide (Jaffer, 2019). Generate a multiple of manifestation effects, including ataxia, hindlimb foot splay, and skeletal muscle weakness (Albedwawi et al., 2022). Being a neurotoxic, Acrylamide may slow down nerve transmission, paralyze the hind limbs of rats, increase the landing foot spread, and cause the animals to drag their feet. In rat primary astrocytes, Acrylamide-induced apoptosis led to mitochondrial dysfunction (Bartkiene et al., 2023).

The key component of life is turmeric, formally known as Curcumin longa, can grow in tropical and subtropical climates all over the world. Curcumin is principally accountable for the bulk of the benefits linked to turmeric, according to a number of researches undertaken over the previous 50 years (Ulaiwi, 2015). Curcumin has a number of health advantages, including anti-inflammatory, antioxidant, anti-coagulant, anti-diabetic, anti-microbial, anti-ulcer, wound-healing, and enhancing fertility properties. It is effective in the treatment of diabetes, a number of malignancies, Alzheimer's disease, and other chronic illnesses (Yavarpour et al., 2019). It has been demonstrated to aid in the treatment of inflammatory diseases, pain brought on by metabolic syndrome, and inflammatory and degenerative eye conditions. (Mansouri et al., 2020) There has been much study on the therapeutic benefits of Curcumin on the neurological syste2m, particularly the brain and the illnesses connected to this vital organ. There has been significant advancement in our understanding of how Curcumin protects against diseases like Alzheimer's and Parkinson's in animal models. There are higher hopes for the use of Curcumin in the treatment of inflammatory brain conditions and brain tumors (Yavarpour et al., 2019).

MATERIALS AND METHODS

Experimental Animals

Thirty mature male Wistar albino rats (aged 8–10) weeks, weighted between 160 and 190) were used in this study. They were acclimatized by spending two weeks prior to the experimental beginning in the animal house of the College of Veterinary Medicine at the University of Baghdad. Throughout the trial, they were kept in plastic cages (3 rats/cage) in a well-ventilated room and were given unrestricted access to a regular pellet food as well as water. The temperature was maintained at 22± 2 ˚C . During the experiment, there was a light/dark cycle with a light on from 7:00 a.m. to 7:00 p.m.. Ethical approval was granted through the local committee of animal care and use at the College of Veterinary Medicine within the University of Baghdad (Number 1508/P.G) before starting this study.

Experimental Design

Group CC: rats were intubated distilled water by gavage needle for 40 days and served as control group.

Group G1: Animals in this group were administered Acrylamide 5mg/kg B.W (Ivanski, et al., 2020). by gavage needle for 40 days.

Group G3: Rats in this group intubated Acrylamide 5mg/kg B.W. every day and Curcumin cumin 100mg/kg B.W(Guo et al., 2020), by gavage needle for 40 days.

Serum Preparation

At the zero time and the end of the experiment, blood samples were taken using the heart puncture technique after the subjects had been given an intramuscular injection of ketamine (60 mg/kg B.W.) and xylazine (40 mg/kg B.W.) to induce anesthesia. Blood samples were placed in non-heparinized gel tubes for 10 minutes before being centrifuged for 15 minutes at 4000 rpm to extract the serum, which was then stored in firmly sealed tubes and kept frozen for the subsequent chemical analysis at -20°C.

Neurobehavioral Tests

Swimming Forced Test

This test was conducted in a glass pool that was 60 cm hight,35 cm width, and 30 cm deepth, and had water that was warmed to 25 C, This test reflects the integration of brain function and neuromuscular by monitoring each animal for (5) min and evaluate duration of time spent as struggling, climbing and reach the complete immobility with head above the water surface (Cryan et al., 2005; Dal-Zotto et al., 2000).

Negative Geotaxis Test

A wooden platform that was slanted at a 45-degree angle was used for this test, and the rat was placed on it with head down on the surface. The taken time by rat to turn 180 degrees was then recorded; the maximum amount of time allowed was 60 seconds (Ruhela, et al., 2019). The platform was cleaned with methyl alcohol 70% for every animal to avoid any olfactory cues.

Y-Maze Test

This test was employed to estimate locomotor activity by performing on a Acrylamide ylic Y-shaped apparatus. The Y-shaped maze has three identical arms, each of 50 cm long, 16 cm wide, and 32 cm wall's hight. The apparatus arms were numbered A, B, and C, the entry into all three arms consecutively was recorded, for instance, if the animal makes the following arm entries ABC, or ACB, or BAC, or BCA, or CAB, or CBA was recorded as successful trail. The test was initiated by placing the rat in the center of the maze (Onaolapo et al., 2012). The maze was cleaned with methyl alcohol 70% for every trail to avoid any olfactory cues.

Statistical Analysis

Graph Pad Prism software version 9.1.0 (San Diego, CA, United States) was used to statistically analyze the obtained data by Two-way ANOVA and One-way ANOVA. When ANOVA was significant, the data were post hoc tested by Tukey's test. Number of animals represented by (n). Data are presented as mean ± standard error (SE). Statistically significant was accepted when P < 0.05 (Kim, 2014).

RESULTS

Effect Of Acrylamide And Curcumin On Body Weight

The body weight did not altered significantly (P≥0.05) between the three groups of animals at the beginning of the experiment (Table 1). However, at the 20 day to the completion of the 40 days of the trial, the body weight in the group of G1 was statistically lower (P < 0.05) than that in the G2 and the CC groups. Moreover, the body weights of rats administered Curcumin increased significantly (P < 0.05) after 20 and 40 days of study compared with G1 animal as.

Table 1: Effect of Acrylamide and Curcumin on Body weight in adult male rats between time Periods, End time vs 20 Days vs zero time for the same group.

Group time	CC	G1	G2
Zero day	180.8± 11.84 Aa	169.7±2 0.46Aa	168.8± 19.40 Aa
20 day	260.7± 28.27Ab	181.5± 16.86 Aa	233.3± 18.81 Cb
40 day	273.5± 30.19 Ab	176.8± 9.88 Aa	240.2± 25.35 Cb

Effect Of Acrylamide And Curcumin On Malondialdehyde

The level of malondialdehyde in the group that received G1 was risen remarkably (P < 0.05) at the end of experiment when it compared with the CC group and the G2 group and when compared with the same group at zero day (Table 2). Moreover, MALONDIALDEHYDE level of Curcumin group was elevated significantly (P<0.05) than CC animals at the end time. However, there were no significant differences (P≥0.05) of this parameter at the beginning of the experiment for the three groups of animals.

Table 2: Effect of Acrylamide and Curcumin on MDA test in adult male rats. Time Periods, (zero time vs End time for the same group).

Group time	CC	G1	G2
Zero time	0.76±0.13Aa	0.80±0.14Aa	0.78±0.17Aa
End time	0.88±0.22Aa	2.74±0.25Bb	1.32±0.19Cb

Effect Of Acrylamide And Curcumin On Total Antioxidant Capacity

There were no significant differences (P≥0.05) in the total antioxidant capacity between the three groups of animals at the beginning of the experiment (Table 3).However at the end of experiment a significant reduction (P<0.05) in TOTAL ANTIOXIDANT CAPACITY was observed only in G1 group compared with G2 and CC groups respectively. Furthermore, Curcumin has enhanced the oxidative status of animals treated with it by significantly increasing (P<0.05) the total antioxidant capacity level even higher that control animals.

Table 3: Effect of Curcumin and Acrylamide TAC test on in adult male rats. time Periods, (zero time vs End time for the same group).

Group time	CC	G1	G2
Zero time	0.96±0.15Aa	0.95±0.11Aa	0.96±0.10Aa
End time	0.95±0.02Aa	0.74±0.04Bb	1.16±0.04Cb

Effect Of Acrylamide And Curcumin In Forced Swimming Test (Immobility Time (Minutes)

At the starting of study, the animals of three groups did not scored any significant differences (P≥0.05) in the time spent to reach complete immobility phase. However, at 40 days of the experiment the G1 rats reaches significantly (p<0.05) faster to immobility than G2 group and CC (Table 4). In addition, there were significantly differences (P<0.05) in G2 groups compared with control group in this parameter at the end of study.

Table 4: Effect of Acrylamide and Curcumin on duration of time spent to reach immobility phase in Forced swimming test in adult male rats. Time Periods, (zero time vs End time for the same group).

Group time	CC	G1	G2
Zero time	2.17±0.09 Aa	2.16±0.15Aa	2.13±0.15Aa
End time	2.23±0.22Aa	1.16±0.07Bb	1.71±0.16Cb

Effect Of Acrylamide And Curcumin In Negative Geotaxis Test

There was statistical increase (P<0.05) in the time taken to turn animal's head 180° in G1 group at the end time when compared with the CC and G2groups at same period and compared with same group at zero time (Table 5), However, there were no significant differences (P≥0.05) between the three groups of animals at the beginning of the experiment.

Effect Of Acrylamide And Curcumin Cumin In Y Maze Test

At 40 days of the experiment the animals exposed to G1 scored significantly lower (p<0.05) number of successful trails compared with the G2 and CC groups at the same period of time and compared with the same animals at the initiating time of experiment (Table 6), However, there were no significant differences (P≥0.05) between the three groups of animals at the beginning of the experiment.

Table 5: Effect of Acrylamide and Curcumin in the time taken to turn animals head 180°in negative geotaxis test in adult male rats. Time Periods, (zero time vs End time for the same group).

Group time	CC	G1	G2
Zero time	5.60±0.57Aa	5.13±0.31Aa	5.23±0.68Aa
End time	5.75±0.77Aa	11.78±0.85Bb	6.70±0.89Aa

Table 6: Effect of Acrylamide and Curcumin on Arms Entry in Y maze test in adult male rats. Time Periods, (zero time vs End time for the same group).

Group time	CC	G1	G2
Zero time	12.00±0.81Aa	11.71±0.75Aa	12.10±0.81Aa
End time	10.42±0.78Ab	6.57±0.53Bb	10.86±0.48Ab

DISCUSSION

According to the Curcumin rent study's findings, oral exposure of Acrylamide to rats significantly reduced their tendency to gain weight. The degenerative abnormalities of central and peripheral neurons, including neurotransmitter, metabolism and the NO signalling system, are likely to be the reason for the reduction in body weight growth brought by Acrylamide exposure (Adani et al., 2020). Furthermore, it has been demonstrated that regular exposure to high doses of Acrylamide might lower hunger motivation and slow the pace of weight gain (Ngo et al., 2021), In addition, Donmez and his team (2020) revealed, that other cause of Acrylamide on body weight gain may be mediated by an increase in oxidative stress. According to our findings, taking Curcumin raised body weight in comparison with the Acrylamide group. Rats receiving Curcumin cumin were protected from weight loss caused by Acrylamide, that's could be due to the ability of Curcumin to reduce oxidative stress by boosting antioxidant enzyme activity and inflammatory factor suppression (Zhanga et al., 2019; Guo et al., 2020; Naemi, el at., 2021), moreover, Curcumin stopped the growth in lipid peroxides, which blocked oxidative damage and reduced toxicity. It has been demonstrated that Curcumin prevents oxidative stress caused by hydrogen peroxide (Ashry et al., 2021).

Malondialdehyde generation rises with Acrylamide and is a significant contributor in the development of oxidative stress. in this research, the 40 days of Acrylamide exposure caused damaging reactions in the tissues of the brain (an important marker of lipid peroxidation and oxidative stress) and reduced total antioxidant capacity with increased malondialdehyde, resulting in lower enzymatic and nonenzymatic antioxidants (Ibrahim et al., 2020). According to the latest results, malondialdehyde concentrations significantly increased due to oxidative stress and excessive ROS generation from Acrylamide, which is in line with earlier studies. Acrylamide is a contributor to redox biology anomalies, particularly oxidative stress. Reactive oxygen species (ROS) cause the oxidative degradation of lipids through a process known as lipid peroxidation, one of the impacts of oxidative stress (Shakir and Saliem, 2021) .The integrity of the membrane transport is lost due to alterations in the lipid structures of the cell membrane layers' liquefaction. The well-known antioxidant actions of Curcumin are due to its phenolic structure, which has electron-capturing characteristics that destabilize ROS. However, Similar to other antioxidants like carotenoids and vitamins (C and E), Curcumin has been found to have dual-edged effects on the quantity of intracellular ROS, which seems to be highly dependent on the type of cell (Hodaei et al., 2019). Multiple cancer cells have been shown to have elevated ROS levels in response to Curcumin, which also possesses antioxidant effects. Moreover, it lowers the blood level of malondialdehyde and has the ability to raise total antioxidant capacity by increase antioxidant capability and shield against oxidative damage in animal tests (Niu et al., 2019).

A study by Ibrahem and colleagues (2020), stated that administration of Acrylamide caused decreased total antioxidant capacity and increased malondialdehyde, resulting in decreased enzymatic and nonenzymatic antioxidants.It is possible to link oxidative stress to a low level of total antioxidants in serum following Acrylamide intoxication, which, is exacerbated by an imbalance between the production and removal of reactive oxygen species and free radicals (Guo et al., 2020). malondialdehyde generation rises with Acrylamide and is a significant contributor in the development of oxidative stress (Sonowal et al., 2017). Furthermore, reduced total antioxidant capacity results in reduced levels of enzymatic antioxidants due to Acrylamide-induced oxidative stress, which produces reactive oxygen species (ROS), lipid peroxidation (LPO), and mitochondrial dysfunction (Farag et al., 2021).The antioxidant properties of Curcumin lower the blood level of malondialdehyde and have the ability to total antioxidant capacity. The effects of Crcumin on oxidative stress markers include the removal of nitrogen and reactive oxygen, regulation of many enzymes, and metal chelation (Kunihiro et al., 2019). In animal studies, Curcumin is frequently utilized to defend against oxidative stress and boost antioxidant capacity; because it can lessen the lipid peroxidation caused by hydrogen peroxide (H2O2), and drastically lowers malondialdehyde when administered. Curcumin's antioxidant effects are attributed to a number of different mechanisms, including inhibition of lipid peroxidation, enhanced glutathione peroxidase activity, increased antioxidant enzyme expression, and improved free radical removal. According to a study that looked at Curcumin impact on malondialdehyde levels (Adibian et al., 2019).

Acrylamide often causes neurotoxicity in animals, which is characterized by impairments in motor function. The duration of time spent striving or climbing, as well as the basic neuromuscular tasks, have all been utilized as indicators of neurotoxicity (Dai et al., 2020). It can be inferred that Acrylamide causes damage to the brain and spinal cord that results in movement disorders similar to those seen in humans by causing circular movements, and other behavioral changes in rodents (Park et al., 2021). Numerous behavioral studies have demonstrated the antidepressant effectiveness of Curcumin in reducing depressed behavior in various animal models. The majority of research noted better results on the forced swimming test (Lamanna et al., 2022). Madiha and colleagues (2019) revealed that post-Curcumin therapy led to effects that were similar to those of an antidepressant, including a reduction in immobility time, an increase in swimming time, and a greater number of leaps.

Acrylamide negatively impacts rat CNS and behaviors, and it also has measurable effects on poor geotaxis performance before other obvious effects. The length of time needed to realign on an inclined surface increased in the animals, when the rats were evaluated on the negative geotaxis test. A range of systems and/or areas, including the cerebellum and muscular strength, may be involved in how Acrylamide affects these activities introducing motor impairments (Senthilkumar et al., 2020).

Curcumin neuroprotective effects were demonstrated by the way it decreased the readjustment time after administration. This test tested neuromuscular coordination, and it showed that injury to the cerebellum caused animals to require less time to realign on an inclined surface. Along with being linked to enhanced amygdala functioning, anxiety and apprehension have a major influence on animals' motor activity (Harika et al., 2022). Curcumin administration significantly shortened the period of acclimatization, demonstrating its neuroprotective effects on neuromuscular coordination. The bioavailability of Curcumin, which is useful in reducing behavioral flaws and altering a number of biochemical parameters, was observed to rise after Curcumin treatment. Increased bioavailability, antioxidant, and neuroprotective qualities may be a result of this protective impact. Additionally, Curcumin is having an effect on brain function and changed negative geotaxis, which are acting centrally by dopaminergic afferent neurons (DAN) (Gazzin et al., 2020). Previous research has shown that dietary Curcumin may be used to treat metal and chemical-induced neurotoxicity in rat brains as well as the impact on CNS cell composition. Despite its poor bioavailability, Curcumin can still be detected in mouse and rat brain tissues after oral dosing (Esquivel et al., 2020).

The modification in brain health, which is a key factor in regulating locomotors activity. It is well known that cells are vulnerable to harm because hazardous substances cause an increase in Reactive Oxygen Species .There were changes in the locomotors activity of rats, according to the Acrylamide influence on motor activity processes in rats. The Y-maze test is frequently used to evaluate learning, memory function, and exploratory behaviors in mice (Senthilkumar et al., 2020). One of the easiest and most trustworthy behavior models is the Y-maze test, which is based on the idea that rodents explore items. Results from the Y-maze showed that Acrylamide was neurologically toxic from the perspective of diminishing memory capacity. Any drug's CNS action is influenced by an animal's locomotor activity. The animal's locomotors activity is taken into consideration when estimating the CNS's level of excitability. Locomotor activity is defined as an increase in alertness, whereas a decrease in locomotor activity indicates a sedative impact. Sedation, which results from CNS depression, and decreased locomotor activity are closely related. Curcumin produced encouraging outcomes and improved spontaneous alternation performance by a percentage. These findings agreed with earlier research. Since it can cross the blood-brain barrier, Curcumin has been shown to interact with and have an impact on a number of target molecules linked to both acute and neuroinflammation. It has also been shown to control the inflammatory response in the central nervous system. Additionally, the research's numerous experimental models of neurodegeneration and neuroinflammation have helped to clarify the neuroprotective therapy employing Curcumin.

CONCLUSION

Acrylamide alters the nuerobehaviors of adult rats by induction oxidative stress and Curcumin restore the normal behaviors and oxidative status.

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NOVELTY STATEMENT

The novelty of the study is focused on physiology and pharmacological Effect of curcumin as an effective neruo-protective, and to reduce the toxicity effect acrylamide on brain of male rats.

AUTHOR CONTRIBUTION

The researchers' effort was equal in accomplishing this task.

CONFLICT INTEREST

There is no conflict of interest.

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