DOI:10.22059/IJVM.2024.374096.1005545 Iranian Journal of Veterinary Medicine Original Article

Online ISSN: 2252-0554`

Nano-curcumin Attenuates Brain Oxidative Stress and Cognitive Deficit in Ketamine-induced Anesthesia in Adolescent Rats

Running title: curcumin ketamine-induced anesthesia

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Abstract

Background: Anesthetics play a crucial role in medical procedures, but some may pose neurotoxic effects, particularly through oxidative stress mechanisms. Ketamine, a widely used anesthetic, has been linked to neurotoxicity characterized by an imbalance in reactive oxygen species (ROS) production and antioxidant defenses.

Objective: This study aimed to investigate the effects of nano-curcumin on ketamine-induced alterations in hippocampal antioxidant components and cognitive functions in adolescent rats.

Methods: In two experiments, sixty male Wistar rats were used. Experiment 1 assessed the biochemical effects of nano-curcumin on ketamine anesthesia, while experiment 2 evaluated its impact on spatial learning and memory. At the end of experiments oxidative stress parameters

such as MDA, SOD, GPx, and CAT were measured. Moreover, Morris water maze test was performed to assess cognitive function.

Result: Biochemical assays revealed that ketamine anesthesia reduced antioxidant enzyme activity and total antioxidant capacity in the hippocampus, while increasing lipid peroxidation. Nano-curcumin treatment alleviated these effects, restoring antioxidant enzyme activity by significantly increasing SOD and CAT levels and reducing lipid peroxidation ($P \leq 0.05$). In the Morris water maze test, ketamine anesthesia impaired spatial learning and memory, which was attenuated by nano-curcumin pretreatment.

Conclusions: In conclusion, nano-curcumin effectively prevented ketamine-induced neurotoxicity by restoring antioxidant balance and ameliorating cognitive deficits. These findings highlight the potential therapeutic utility of nano-curcumin in mitigating anesthesia-induced neurotoxicity and emphasize the importance of oxidative stress in anesthesia-related neurological complications.

Keywords: Anesthesia, Brain, Ketamine, Nano-curcumin, Oxidative stress

1. Introduction

Anesthetics are employed in medical procedures to induce anesthesia. While most anesthetics are considered safe, some may have neurotoxic effects, even at standard doses. There are incompatible findings regarding the impact of anesthetics on neuronal function and development. Different anesthetics and anticonvulsant medications have been found to cause neuronal injury, dysfunction, and apoptosis both in laboratory settings and in living organisms (Alam *et al.*, 2017, Quiroz-Padilla *et al.*, 2018, Clausen *et al.*, 2019, Hajizadeh *et al.*, 2018). However, the mechanisms through which anesthesia brings about these changes are not well understood. One prominent theory is that the onset of oxidative stress may trigger neuroapoptosis (Stevens *et al.*, 2019, Resae *et al.*, 2022), initiating a chain reaction of adverse neurological consequences. Under such circumstances, there is an escalation in the generation of reactive oxygen species (ROS). Oxidative stress is triggered by an imbalance between free radical generation, mainly ROS and nitrogen reactive species (RNS) (Barfourooshi *et al.*, 2023, Chukwu *et al.*, 2023, Shahsavari *et al.*, 2023). Ordinarily, ROS is a routine outcome of brain cell metabolism. Yet, their buildup during oxidative stress can overpower the brain's innate protective antioxidant mechanisms, resulting in cellular impairment and demise (Gascoigne *et al.*, 2022). Extensive research indicates that reactive oxygen species (ROS) play a significant role in the development of various diseases, particularly neurological and psychiatric disorders, given the brain's

heightened susceptibility to oxidative harm (Singh *et al.*, 2019, Ng *et al.*, 2008). Moreover, oxidative stress has been implicated in aging, inflammation, cancer, degenerative conditions (Hussain AlDulaimi, 2024, Liguori *et al.*, 2018), as well as exposure to xenobiotics and medications, including anesthetics (Lee *et al.*, 2015). Anaesthetic-induced oxidative stress can affect lipids, proteins, and DNA (Alavuk Kundović *et al.*, 2020). Therefore, it is crucial to select anesthetics that minimize oxidative stress to prevent further tissue damage.

Ketamine, a short-acting blocker of NMDA receptors, has been widely utilized as an anesthetic since the 1960s. Chemically, it is identified as [2-O-chlorophenyl-2-(methylamino)cyclohexanone] (Moghaddam, 2021), belonging to the phencyclidine derivative class. Initially hailed as an ideal anesthetic due to its ability to fulfill all essential components of surgical anesthesia (such as pain relief, immobility, amnesia, and loss of consciousness) (Annetta *et al.*, 2005). Ketamine exerts its pharmacological effects by modulating neurotransmission at postsynaptic receptors, including N-methyl-D-aspartate (NMDA) glutamate receptors and gamma-aminobutyric acid (GABA) receptors. Functioning as an uncompetitive antagonist, ketamine blocks NMDA receptors, leading to dissociative anesthesia (Zhou and Duan, 2023). Notably, studies in humans have indicated that ketamine can induce neurotoxicity via oxidative stress mechanisms (Reus *et al.*, 2017). In rodent models, ketamine prompts a compensatory

overexpression of NMDA receptors and elevates Ca2+ levels (Li *et al.*, 2018), resulting in Ca2+ accumulation, which in turn leads to mitochondrial excitotoxic injury and the generation of reactive oxygen species (ROS) (Li *et al.*, 2018, Liu *et al.*, 2013). Additionally, research by Oliveira et al. demonstrated that various sub-anesthetic doses of ketamine affect lipid peroxidation and tissue protein oxidation in multiple cerebral structures (de Oliveira *et al.*, 2009).

Turmeric (Curcuma longa), a member of the Zingiberaceae family, has been used for centuries throughout Asia as a food additive and traditional herbal medicine. Epidemiological evidence supports a link between better cognitive functionin elderly Asians and curry consumption with turmeric (Assi *et al.*, 2023). Curcumin is the major yellow polyphenol present in the rhizomes of turmeric (Khayatan *et al.*, 2022, Banji *et al.*, 2021, Kaboutari *et al.*, 2023, Tamadonfard *et al.*, 2010). Studies indicate that curcumin has several properties, including antioxidant, anti-infection, anti-tumor characteristics and neuroprotective potential (Khayatan *et al.*, 2022, Godse *et al.*, 2023, Gholipour-Shoshod *et al.*, 2023). Curcumin exhibits potent anti-inflammatory properties by reducing the production of inflammatory cytokines such as interferon-γ, TNF-α, IL-1, and IL-6, as well as inhibiting cyclooxygenase-2 (COX-2) activity (Kahkhaie *et al.*, 2019). However, its health benefits are limited due to its low water solubility, rapid metabolism, and quick elimination from the body (Hewlings and Kalman, 2017). Curcumin, being a hydrophobic

natural polyphenol, has low solubility in aqueous solvents but higher solubility in organic solvents (Maiti and Dunbar, 2018). Additionally, curcumin readily transforms into hydrophilic metabolites, which can impede its absorption (Jäger *et al.*, 2014). Consequently, curcumin is poorly absorbed from the gut, resulting in low bioavailability and negligible serum levels when taken alone. To address this issue, various delivery systems such as nanoparticles (e.g., poly lactic-co-glycolic acid (PLGA) nanoparticles, lipid-based nanoparticles, nanosuspensions, lipid-PLGA nanobubbles, and nanoemulsions), ultrasound-targeted microbubbles, micelles, dendrimers, and exosomes have been developed to enhance curcumin's physicochemical properties, bioavailability, and pharmacokinetics (Panzarini *et al.*, 2020, Mohammed *et al.*, 2021, Ashjazadeh *et al.*, 2019) Nanoparticles of curcumin protect it from metabolism and enhance its stability, prolonging its time in the bloodstream (Moballegh Nasery *et al.*, 2020). In light of this evidence, the current study aimed to assess the effects of nano-curcumin on ketamine-induced alterations in hippocampal antioxidant components and cognitive functions.

2.Materials and Methods

2.1.Animals

Sixty male Wistar rats (200 to 220g) obtained from the Laboratory Animal Center (Medical University of Lorestan) were used in the study. Rats were kept under controlled conditions of 23 ± 2° C and light conditions for 12 h of light and 12 h of darkness in the animal house of the Faculty of Veterinary Medicine affiliated with Lorestan University. All animals were allowed free access to standard chow diet and tap water *ad libitum*. All experiments were carried out in accordance with the recommendations of the Animal Care Committee for the Lorestan University (Khorramabad, Iran) with approval number LU. ECRA.2023.22.

2.2.Experimental design

Experiment 1 was conducted to assay the effects of nano-curcumin on biochemical alterations following anesthesia with ketamine. In this experiment forty rats were divided into two groups: curcumin treated (T) and normal saline received (S) groups. Each of these groups had four subgroups: T1-T4 and S1-S4 (n = 5 per subgroup) (table 1). The animals in groups T1-T4 were subjected to daily gavage of nano-curcumin 20.00 mg kg-1 (Sina Curcumin capsule, each capsule contains 80.00 mg curcumin as nano micelle, these spherical nanomicelles have a particle size of about 10 nm) for 2 weeks and groups S1-S4 were received normal saline for the same duration. At the last day of administration, all groups except groups T4 and S4 were

anesthetized with ketamine. Rats in groups T1, T2 and T3 were euthanized immediately, 4 and 12 hours after anesthesia, respectively, and their hippocampus were taken for biochemical examinations. A similar protocol was performed for anesthesia and brain tissue collection in groups S1, S2, and S3. Groups T4 and S4 were not anesthetized but they were also sampled following cervical dislocation without ketamine injection. The dose of nano-curcumin (20 mg/kg) was determined based on our pilot study. All of the treatments were applied intraperitoneal injection.

Table 1: Experimental design in experiment 1.

Groups		Time of Sample collection after anesthesia (hour)
Curcumin Treated	T1	0
	T2	4
	T3	12
	T4	without anesthesia
Normal Saline	S1	0
	S2	4
	S3	12

S4 without anesthesia

Experiment 2 was designed to investigate the effects of nano-curcumin on spatial learning and memory after anesthesia with ketamine. In this experiment twenty rats were divided into four groups (n = 5 per group) in the order listed below:

Group I-received normal saline without anesthesia (control)

Group II-received normal saline with anesthesia (ketamine)

Group III-received nano-curcumin without anesthesia (curcumin)

Group IV-received nano-curcumin with anesthesia (curcumin+ketamin)

All injections were given IP once a day for two weeks. The dose of curcumin used was 20 mg/kg. The rats in groups II and IV were anesthetized with ketamine on the last day of injections. All rats were introduced to the MWM test after recovery from anesthesia for evaluation of spatial learning and memory.

2.3.Biochemical estimations

The rats were sacrificed by cervical dislocation under ether anesthesia at sample collection times and the hippocampus was dissected on an ice-cold surface. Tissue homogenates were prepared as described by Carrillo et al. (1991) (Carrillo *et al.*, 1991). Supernatants were recovered and stored at -70°C until MDA levels (an indicator of lipid peroxidation), SOD, CAT, and GPx enzyme activities, and TAC were determined.

2.4.Measurement of lipid peroxidation

The level of lipid peroxidation was indicated by the content of MDA in the hippocampus using biochemical commercial kits (Asan, Khorramabad, Iran).

2.5.Determination of GPx and SOD activities

SOD and GPx activities were measured in the supernatant by using Asan kits (Khorramabad, Iran) according to the manufacturer's instructions. The GPx and SOD activities were expressed as milliunits per milligram of tissue protein (mU/mg protein).

2.6.Determination of CAT activities

CAT concentration was measured using Asan commercial kits (Khorramabad, Iran).

2.7.Protein measurement

Protein content of tissue homogenates was determined using a colorimetric method of Lowry with bovine serum albumin as standard (Classics Lowry *et al.*, 1951).

2.8.Morris water maze testing

Evaluation of hipocampal-dependent spatial learning and memory was performed by standard Morris water maze task (Morris *et al.*, 1982). The one-day water maze test as described previously (Frick *et al.*, 2000) with minor modifications was carried out. This version of the water maze test was chosen for practical reasons as it could rapidly evaluate learning and memory in rodents. The water maze consisted of a circular tank (190cm in diameter) and filled with water (up to 30cm deep; temperature: 22±2 °C). The tank was divided into four zones and a platform (18cm×18cm) was submerged 2cm below the water surface in one of these zones. Any improvements in spatial learning and memory are confirmed by the spatial acquisition and probe trial respectively. In the first test (spatial acquisition), each rat underwent three blocks of 4 swims separated by a 30-minute interval. In the swimming trials, each rat was released gently into the water at a randomly chosen quadrant. The rat swam and learned how to find the hidden platform within 60 s. After reaching, the rat was allowed to stay on the platform for 10 s and was

then taken back into the cage. The rats were placed on the platform by hand for 10 s if they could not escape to the platform within 60 s by themselves, and their escape latency was accepted as 60 s. The time to reach the platform (latency), the length of swim path, and the swim speed were recorded by a video tracking system. In the second test (probe trial) which was conducted after a 30- min break, the platform was removed and the rats undergoing a single trial of 60s. The percentage of time spent in each zone including the correct quadrant was recorded. After the end of each block, all animals were put back into their cages to rest.

2.9.Statistics

All data were analyzed using the SPSS for Windows (Version 24). To compare the data on SOD, CAT, or GPx enzyme activities and TAC and MDA levels, one-way ANOVA and post-hoc *Tukey's* test was used. The escape latencies, pathlength, and swim speed in the water maze were analyzed by two-way ANOVA for between-subjects differences between nano-curcumin and normal saline ("curcumin" effect) and repeated measures (within subjects) effects across block interval 1 to 3 ("BLOCK" effect). The probe trial data for the percentage of time spent in each of the four zones were analyzed by multivariate ANOVA. The results of the experiments were expressed as means ± SEM. A $P \leq 0.05$ value was considered to be statistically significant.

3.Results

According to Figure 1, ketamine anesthesia significantly reduced levels of GPx compared to the non-anesthetized group ($P \leq 0.05$). Treatment with Curcumin increased levels of GPx, but no significant difference was observed ($P \leq 0.05$).

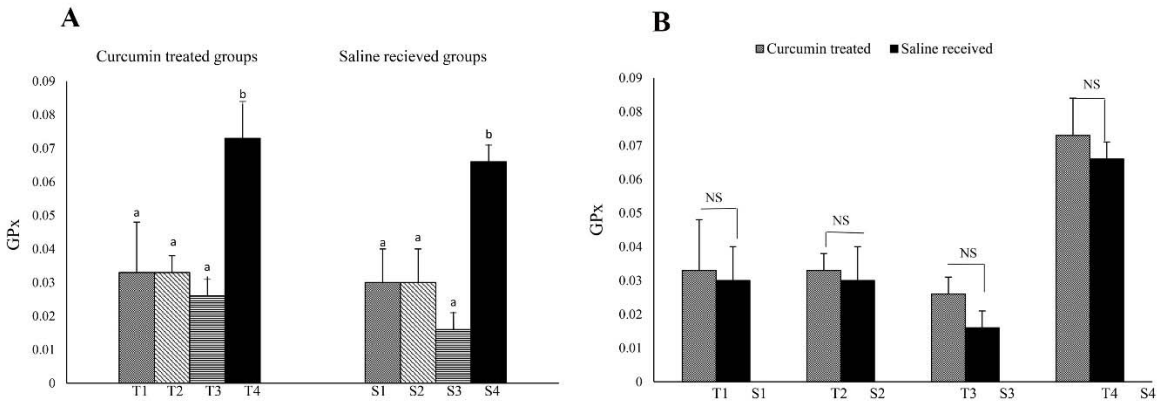

Figure 1: Evaluation of glutathione peroxidase (GPx) in experimental groups of the study. A: Comparison between anesthetized and non-anesthetized groups of curcumin and saline treated. B: Comparison between curcumin and saline treatment groups of the same time frame.

Anesthesia significantly reduced levels of CAT compared to the non-anesthetized group ($P \leq 0.05$) (Figure 2A). Curcumin increased the amount of CAT in the treatment groups; however, a significant increment was only observed for the T3 group ($P \leq 0.05$) (Figure 2B).

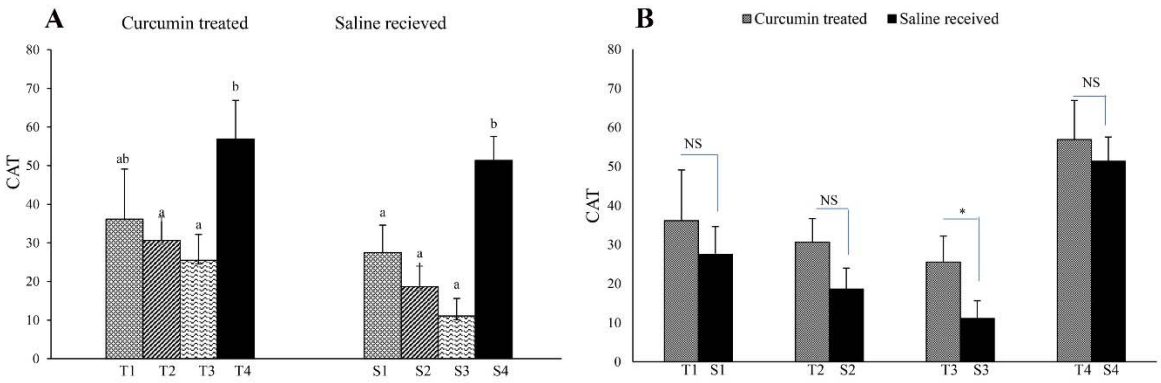

Figure 2: Evaluation of catalase (CAT) in experimental groups of the study. A: Comparison between anesthetized and non-anesthetized groups of curcumin and saline treated. B: Comparison between curcumin and saline treatment groups of the same time frame.

Based on Figure 3A, In the T groups, no significant difference was observed between the anesthetized and non-anesthetized groups with ketamine. While in the saline-treated groups, ketamine anesthesia significantly decreased levels of SOD ($P \leq 0.05$). Based on Figure 3B, the T3 group significantly increased the level of SOD compared to the S3 group ($P \leq 0.05$).

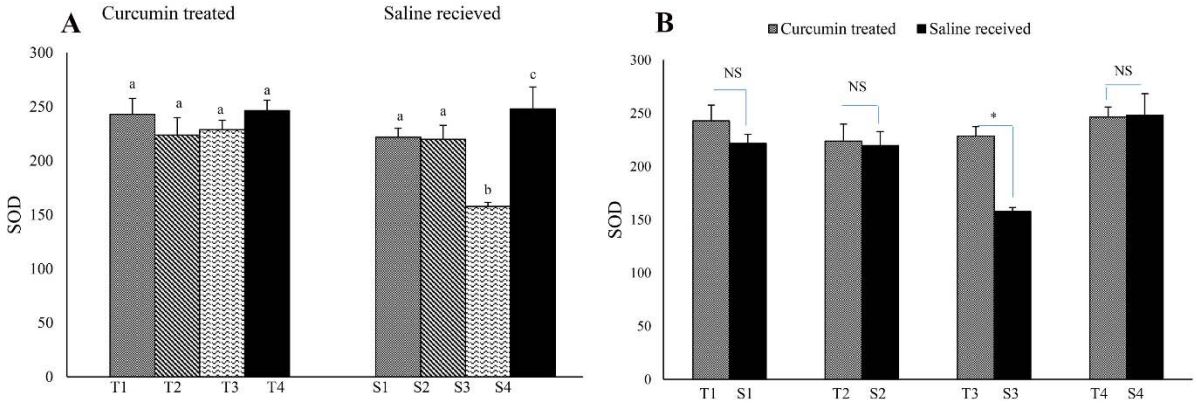

Figure 3: Evaluation of superoxide dismutase (SOD) in experimental groups of the study. A: Comparison between anesthetized and non-anesthetized groups of curcumin and saline treated. B: Comparison between curcumin and saline treatment groups of the same time frame.

Anesthesia significantly reduced TAC levels when compared to the T4 and S4 groups in which did not receive anesthesia ($P \leq 0.05$) (Figure 4). No significant difference was observed between the curcumin and saline-treated groups for TAC (Figure 4B).

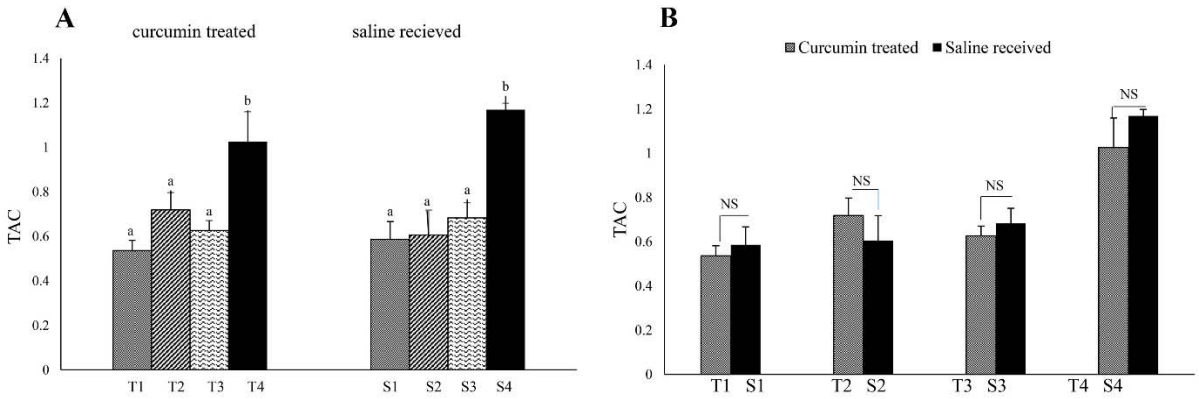

Figure 4: Evaluation of total antioxidant capacity (TAC) in experimental groups of the study. A: Comparison between anesthetized and non-anesthetized groups of curcumin and saline treated. B: Comparison between curcumin and saline treatment groups of the same time frame.

Following ketamine anesthesia, MDA significantly reduced ($P \leq 0.05$) (Figure 5A). MDA decreased in the curcumin-treated groups, but it was not significant ($P > 0.05$) (Figure 5B).

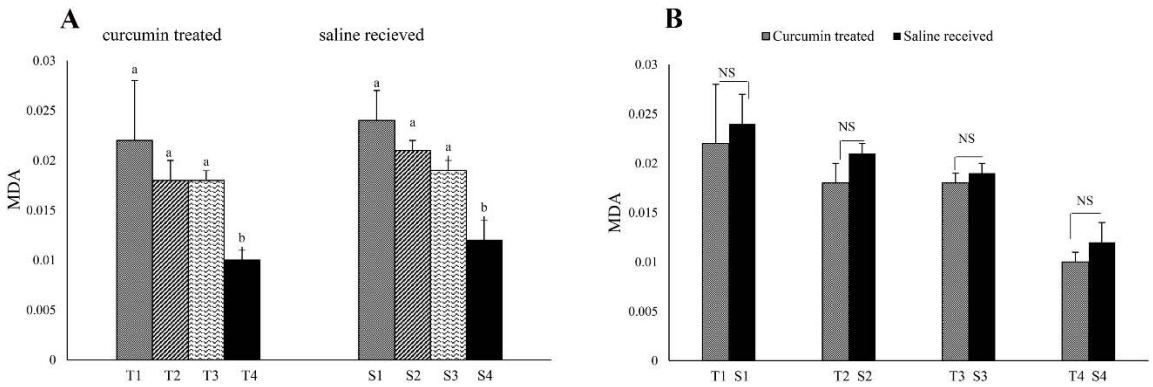

Figure 5: Evaluation of malondialdehyde (MDA) in experimental groups of the study. A: Comparison between anesthetized and non-anesthetized groups of curcumin and saline treated. B: Comparison between curcumin and saline treatment groups of the same time frame.

The results of latency time are provided in Figure 6. Based on the graph, anesthesia with ketamine significantly increased the latency time compared to the control group without anesthesia ($P \leq 0.05$). The curcumin-treated group significantly reduced latency time in comparison to the control group ($P \leq 0.05$). In the ketamine+curcumin treated group; latency time was significantly lower than that of the ketamine group ($P \leq 0.05$).

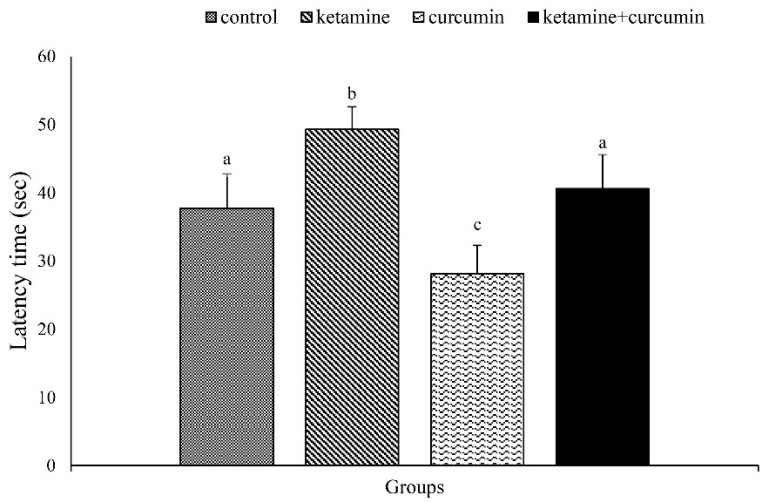

Figure 6: Effect of ketamine and nano-curcumin treatment on spatial learning as measured by the MWM task. Escape latency to reach the hidden platform in rats received ketamine enhanced compared with the control group. Meanwhile, nano-curcumin administration significantly reversed ketamine-induced impairment. There are significant differences between groups with different superscripts in a column (a,b, and c ; $P \leq 0.05$). Each point is the mean±SEM.

Results for time spent in the target zone (%) are indicated in Figure 7. Based on the graph, anesthesia by ketamine significantly reduced the time spent in the target zone compared to the control group ($P \leq 0.05$). Although ketamine and ketamine+curcumin groups increased the time spent in the target zone, it was not significant when compared to the ketamine group ($P > 0.05$).

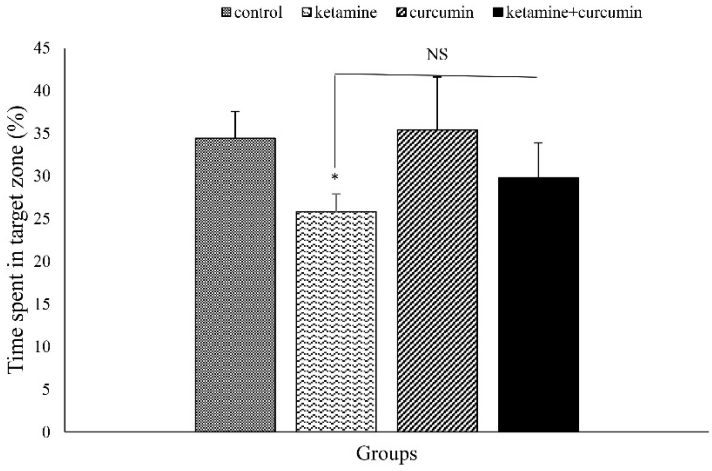

Figure 7: Effect of ketamine and nano-curcumin treatment on memory retention, as measured by the MWM task. Mean time spent by rats in the target zone decreased significantly in the ketamine group in compared to the control group. Administration of nano-curcumin could

improve the impairment in memory caused by ketamine. *Represents the significant difference between ketamine with control groups. (*$P \leq 0.05$), NS: non-significant.

4.Discussion

The current research demonstrates that administering curcumin (20 mg/kg, for 14 days), an active compound found in turmeric (Curcuma longa), to rats prior to exposure to ketamine effectively prevented the behavioral and pro-oxidant effects induced by ketamine in adolescent rats. The behavioral and biochemical impacts of ketamine appear to be contingent upon dosage. Studies have revealed that low doses of ketamine (5–10 mg/kg) possess antidepressant properties (Katalinic *et al.*, 2013). Conversely, moderate doses (10–50 mg/kg) of ketamine can lead to hyperlocomotion and cellular dysfunction (Sedky and Magdy, 2021) , while higher doses result in anesthetic and dissociative effects. Gazal et al. (2014) demonstrated that administering ketamine (25 mg/kg) for 8 days induces hyperlocomotion in the open-field test and oxidative damage in the prefrontal cortex (PFC) and hippocampus (HP) (Gazal *et al.*, 2014). Furthermore, another study found that administering a sub-anesthetic dose of ketamine alters oxidative stress parameters in the rat brain. Da Silva et al. (2010) demonstrated increased lipid peroxidation and nitrite content in the cortex of mice following a single dose of ketamine (da Silva *et al.*, 2010). In

preclinical models, non-anesthetic doses of ketamine can induce hyperlocomotion, stereotypy, impaired cognitive function, and social interaction (Gazal *et al.*, 2014). It's worth noting that in the current study, the anesthetic dose of ketamine (75 mg/kg, intraperitoneal) and its acute effects on behavioral and neurochemical changes were assessed.

An imbalance in oxidation-reduction processes within living organisms leads to an accumulation of reactive oxygen species (ROS), resulting in oxidative stress (Costantini, 2019). To counteract this, organisms employ various antioxidant defense mechanisms. Enzymatic antioxidants include superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GR). SOD, a key player in ROS defense, facilitates the conversion of superoxide anions (O2-) into hydrogen peroxide (H2O2) and molecular oxygen (O2) (Carmo de Carvalho e Martins *et al.*, 2022). Subsequently, H2O2 can react with iron to generate highly reactive hydroxyl radicals (Halliwell and Gutteridge, 2015). CAT then converts H2O2 into water and O2, completing the detoxification process. (Cecerska-Heryć *et al.*, 2022). Neuronal cells are particularly susceptible to oxidative damage due to their heightened oxygen consumption, relatively weak antioxidant defenses (Cobley *et al.*, 2018) , and the abundance of polyunsaturated fatty acids in their membranes. Specifically, the lipid composition of neuronal membranes is rich in polyunsaturated fatty acids, rendering them more vulnerable to oxidative

stress. Elevated levels of reactive oxygen species (ROS) have detrimental effects on various cellular processes such as signal transduction, structural plasticity, and cellular resilience, primarily by inducing lipid peroxidation in membranes and damaging proteins and nucleic acids (Mahadik *et al.*, 2001). Moreover, mitochondria in presynaptic terminals are exposed to elevated calcium levels from voltage-gated calcium channels, accelerating oxidative damage at synaptic sites (Grimm and Eckert, 2017). Our study revealed that ketamine induces changes in certain oxidative stress parameters, such as an increase in malondialdehyde (MDA) levels and a decrease in total antioxidant capacity in the hippocampus (HP) of rats. In our experiment, ketamine administration resulted in reduced activity of antioxidant enzymes such as glutathione peroxidase, superoxide dismutase, and catalase in the hippocampus. Previous studies have documented the effects of ketamine on lipid peroxidation in various brain regions (Brocardo *et al.*, 2010). The hippocampus, a critical structure within the limbic system, plays a pivotal role in cognitive functions such as learning, memory consolidation, and recall of declarative memories (Eichenbaum, 2001). It is particularly important for spatial memory map formation (Papp *et al.*, 2007). Research has shown that decreased hippocampal lipid peroxidation enhances spatial cognition and learning memory (Gamoh *et al.*, 2001), while increased antioxidative activity in the hippocampus prevents (Hashimoto *et al.*, 2002) or mitigates (Hashimoto *et al.*, 2005)

impairments in learning ability in rats. Furthermore, preclinical evidence suggests that ketamine exerts rapid effects on synaptogenesis in the hippocampus, a brain region strongly implicated in memory consolidation (Kandlur *et al.*, 2020).

Consistent with a study conducted by Gazal et al. (2014), our findings suggest that curcumin effectively prevents cognitive deficits and alterations in oxidative stress parameters induced by ketamine in rats. Numerous studies have highlighted the anti-inflammatory and antioxidant properties of curcumin (Peng *et al.*, 2021, Vaiserman *et al.*, 2020). It has been demonstrated that curcumin can normalize levels of cellular antioxidant enzymes, including SOD and catalase, and reduce oxidative stress in cellular models of Alzheimer's disease (Huang *et al.*, 2012). Indeed, due to its antioxidative properties, curcumin has shown promise in preclinical models of various conditions, including neurodegenerative disorders, depression, and aging (Menon and Sudheer, 2007). Consistent with these findings, our study showed that curcumin improves learning impairments in ketamine-treated rats. There is abundant evidence indicating that curcumin administration can enhance memory function, cerebral blood flow (Rajasekar *et al.*, 2013) , and elevate levels of brain-derived neurotrophic factor (BDNF) and hippocampal neurogenesis (Xu *et al.*, 2007). Researchers have explored the connection between curry consumption, containing curcumin, and cognitive function. Individuals who consumed curry occasionally (less than once

a month) or often (more than once a month) exhibited better performance on cognitive function tests compared to those who rarely or never consumed curry (Mishra and Palanivelu, 2008). In a previous study, we demonstrated that an herbal extract with antioxidant properties improved spatial memory impairment induced by ethanol (Taati *et al.*, 2011). Considering the hippocampus's role in spatial learning and its susceptibility to oxidative damage induced by ketamine (Gazal *et al.*, 2014), it is evident that oxidative stress plays a role in ketamine-induced cognitive impairments in spatial water maze performance. To our knowledge, there have been no reports on the effects of curcumin on spatial learning and memory in ketamine-treated adolescent rats. In this study, pretreatment with curcumin significantly reduced latency time and mitigated ketamine's effects on learning performance compared to the ketamine-only group. These findings suggest that co-treatment with curcumin ameliorates ketamine-induced memory deficits during the acquisition process in rats. However, it did not significantly affect the retrieval process of spatial memory performance. Previous research has shown that antioxidant components of plants can enhance cognitive function (Renis *et al.*, 1996, Bisson *et al.*, 2008, Kumar *et al.*, 2009, Khalili *et al.*, 2009, Farshchi *et al.*, 2010, Juyal *et al.*, 2010). In conclusion, our findings suggest that the improvement in spatial memory deficits induced by ketamine may be attributed to the antioxidant properties of curcumin.

Acknowledgments

The authors would like to thank vice chancellor of research of Lorestan University for their support.

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نانو کورکومین استرس اکسیداتیو مغز و نقص شناختی را در بیهوشی ناشی از کتامین در موش های صحرایی نوجوان کاهش می دهد.

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چکیده

زمینه مطالعه: داروهای بیهوشی نقش مهمی در روش‌های درمانی پزشکی دارند، اما برخی از آنها ممکن است اثرات نوروتوکسیک، به‌ویژه از طریق مکانیسم‌های استرس اکسیداتیو داشته باشند. کتامین، یک داروی بیهوشی پرمصرف، با سمیت عصبی مرتبط است که با عدم تعادل در تولید گونه های فعال اکسیژن (ROS) و دفاع آنتی اکسیدانی مشخص می شود.

هدف: این مطالعه با هدف بررسی اثرات نانو کورکومین بر تغییرات ناشی از کتامین در اجزای آنتی اکسیدانی هیپوکامپ و عملکردهای شناختی در موش های صحرایی نوجوان انجام شد.

روش کار: در دو آزمایش از 60 سر موش صحرایی نر نژاد ویستار استفاده شد. آزمایش 1 اثرات بیوشیمیایی نانو کورکومین را بر بیهوشی کتامین ارزیابی کرد، در حالی که آزمایش 2 تأثیر آن را بر یادگیری فضایی و حافظه ارزیابی کرد. در پایان آزمایش پارامترهای استرس اکسیداتیو مانند MDA، SOD، GPx و CAT اندازه‌گیری شد. همچنین برای ارزیابی عملکرد شناختی، آزمون ماز آبی موریس انجام شد.

نتایج: سنجش‌های بیوشیمیایی نشان داد که بیهوشی کتامین باعث کاهش فعالیت آنزیم آنتی‌اکسیدانی و ظرفیت آنتی‌اکسیدانی تام در هیپوکامپ و افزایش پراکسیداسیون لیپیدی می‌شود. تیمار نانو کورکومین این اثرات را کاهش داد، فعالیت آنزیم آنتی اکسیدانی را با افزایش معنی دار سطوح SOD و CAT و کاهش پراکسیداسیون لیپیدی بازیابی کرد ($P\leq0.05$). در آزمایش ماز آبی موریس، بیهوشی کتامین باعث اختلال در یادگیری و حافظه فضایی شد که با پیش درمانی نانو کورکومین کاهش یافت.

نتیجه‌گیری نهایی: در نتیجه، نانو کورکومین با بازگرداندن تعادل آنتی‌اکسیدانی و بهبود نقایص شناختی به طور مؤثری از سمیت عصبی ناشی از کتامین جلوگیری کرد. این یافته‌ها کاربرد بالقوه درمانی نانو کورکومین را در کاهش سمیت عصبی ناشی از بیهوشی برجسته می‌کند و بر اهمیت استرس اکسیداتیو در عوارض عصبی مرتبط با بیهوشی تأکید می‌کند.

کلمات کلیدی: بیهوشی، مغز، کتامین، نانو کورکومین، استرس اکسیداتیو