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Effects of Camel Milk on Antioxidant Activity in Rats with Valproic Acid-induced Autism

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ABSTRACT

Introduction: Autism spectrum disorder refers to a wide range of nervous system disorders. Autistic patients often have a defective antioxidant defense system and manifest symptoms of impaired cognitive interaction. Camel milk has numerous beneficial nutrients and has been used in the treatment of autism. The present study aimed to investigate the effects of camel milk on the antioxidant activity and enzymes of autistic rats.

Methods: Pregnant rats were intraperitoneally injected on embryonic day 12.5 with valproic acid (VPA; 500 mg/kg) to induce an autistic state. In addition, 18 male offspring rats were injected with risperidone (0.2 mg/kg) three times per week. Six of these cases were fed daily with raw camel milk (10 ml/kg), and six others were fed with pasteurized camel milk for 42 days. Social interaction and repetitive behaviors were measured using the Y-maze based on catalase (CAT) activity, glutathione (GSH) level, and superoxide dismutase (SOD) activity at the outset and after the treatment period.

Results: Behavioral symptoms (impaired social interaction and repetitive behaviors) were evident after VPA administration. After receiving treatment, impaired social interaction and repetitive behaviors significantly improved in the autistic rats ($P<0.01$). In addition, VPA enhanced the oxidative stress status in the biochemical tests ($P<0.001$), and camel milk increased CAT activity ($P<0.001$), GSH level ($P<0.05$), and SOD activity ($P<0.0001$).

Conclusion: According to the results, camel milk could recover the VPA-induced impairment of social interaction and repetitive behaviors in the autistic rats and improve the defects in their antioxidant defense system.

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Introduction

Autism spectrum disorder (ASD) refers to a wide range of nervous system disorders. Autism is often characterized by impaired social interaction, repetitive and aimless physical behaviors, and a general lack of interest and activity (1). Evidence suggests that exposure to antiepileptic medicines such as valproic acid (VPA) during pregnancy could increase the risk of ASD in children (2). Among the models developed for autism, the VPA animal model encompasses the most similar symptoms to human ASD (3). According to the literature, the pregnant animals who are exposed to VPA during the first trimester of pregnancy are at a high risk of giving birth to autistic cubs (4).

An autism model based on the induction period could be established on various embryonic (E) days in animals, and E-12.5 day has been suggested for VPA exposure in rats (5). According to the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition), ASD is primarily characterized by repetitive behaviors and impaired social interaction (9). These symptoms are assessed by several behavioral tests, including sniffing

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(social interaction) and Y-maze (repetitive behaviors) (6). Repetitive behaviors in VPA-exposed rats are associated with the increased re-entry of the same earlier-traveled arm in the Y-maze (7). Some non-pharmacological agents have proven effective in the treatment of major ASD symptoms (8). For the treatment of ASD-related mood disorders, antipsychotic drugs such as risperidone and aripiprazole have been approved by the US Food and Drug Administration (FDA) (9).

Reactive oxygen species (ROS) such as superoxide radicals ($^{\bullet}O_2^-$ ،$^{\bullet}$ OOH), peroxyl (ROO), and hydroxyl ($^{\bullet}$ O.H.) are produced due to oxidative stress (10). Several studies have confirmed that oxidative stress contributes to the development of autism in patients with ASD (11, 12). Moreover, high levels of cytokine and xanthine oxidase have been detected in the blood flow of the autistic patients producing free radicals. Previous studies have shown the blood-brain barrier leakage in autism, which indicates susceptibility to oxidative damage. Excessive stimulatory receptors in autistic patients also cause oxidative damage to the nerve cells, while also increasing oxidative stress via glutamate secretion (13). The increased number of ROS in the brain and blood plasma reduces the brain cells, thereby leading to cell damage, apoptosis, and ultimately autism (14). Cell ROS are neutralized by antioxidant defense mechanisms, including catalase (CAT), superoxide dismutase (SOD), and glutathione (GSH) enzymes (14, 15).

Camel milk contains multiple valuable nutrient and is a popular product among different populations owing to its therapeutic properties and disease prevention mechanisms (16). Some of the most prominent qualities of camel milk are low levels of fat, cholesterol, and lactose and high levels of minerals (e.g., calcium, iron, copper, zinc, magnesium, potassium), vitamins (A, C, group B). Furthermore, camel milk contains high levels of lactoperoxidase, immunoglobulin G, and secretory immunoglobulin A, which distinguish it from the milk of other mammals (17) and add to the its significant antioxidant effects (18). Camel milk has been reported to improve several diseases, such as diabetes, allergies, immune disorders, hepatitis, autism, and cancers (19-21). In some countries, it is traditionally used for the treatment of autism. Previous studies regarding autism have indicated that camel milk could significantly improve autistic symptoms (21, 22).

The present study aimed to investigate the effects of a diet containing camel milk and risperidone on some of the behavioral symptoms of autism using social interaction and Y-maze tests. Another objective was to measure the antioxidants in camel milk and evaluate the activity of SOD, GSH, and CAT in the adult offspring of autistic rats.

Materials and Methods

Experimental Animals

In this study, Wistar rats were provided by the laboratory of the Animal Center of Mashhad University of Medical Sciences, Iran. The rats were kept in plastic polycarbonate cages at the relative humidity of 55±5% and room temperature (25±2°C) within a 12-hour light/dark cycle. The animals received standard pellets and had access to drinking water. Animal handling was in accordance with the guidelines of the Health Research Ethics Committee of Mashhad University of Medical Sciences (I.R.MUMS.MEDICAL.REC.1398.264).

In total, five female rats and one male rat were placed in each cage, and a vaginal smear was collected to detect pregnancy plaques twice per day (8:30 PM and 8:30 AM). Afterwards, the rats were transferred to separate cages on the first day of pregnancy (GD1).

Preparation of Rat Model of VPA-induced Autism

After pregnancy, the rats were randomly divided into two group sets (n=5, n=2). Group one (five females) was intraperitoneally injected with VPA (500 mg/kg), and group two (two females) was intraperitoneally injected with normal saline on GD12.5 (7, 23).

Initially, VPA was dissolved in a 0.9% saline solution, and the injection volume was determined to be 10 milligrams per kilogram of the body weight. All the rats were maintained until the weaning of the offspring on a postnatal day (PND21). Following that, 30 male pups (six per group) were weaned and grouped for the postnatal experiments. The naïve group included the rats whose mothers did not receive VPA, the VPA group included the rats whose mothers received VPA without a treatment, and the risperidone group included the rats whose mothers received VPA and risperidone. In the

camel raw milk and risperidone group, the animals received raw milk and risperidone after VPA exospore. In the pasteurized camel milk and risperidone group, the animals received pasteurized milk with risperidone after VPA exposure. In line with the previous studies in this regard, only male offspring was injected with VPA to demonstrate social interaction deficiency and higher prefrontal dopamine system activity (23).

The reason for using two types of camel milk was that pasteurization is performed at the temperature of 72°C for 16 seconds to kill bacteria. On the other hand, the general denitrification of proteins occurs at the average temperature of 55-85°C. Therefore, it is hypothesized that the efficiency of some proteins may diminish in camel milk, while casein has been reported to have a higher temperature resistance. Notably, raw milk has been reported to contain germs that cause some diseases, such as malaria.

Treatment Administration

In the treatment intervention, we used risperidone (Sobhan Darou Co.) and raw and pasteurized camel milk to assay their impact on autistic symptoms. Initially, risperidone was dissolved in a saline solution containing less than 0.1% v/v acetic acid and injected intraperitoneally (0.2 mg/kg); dosage of the drugs was determined based on previous studies (24).

Raw and pasteurized milk were administered to the rats daily (10 ml/kg) using a nasogastric needle. Treatment duration was 42 days (days 35-77). Behavioral tests were performed on PND30-35 before the treatment and on the last day of the treatment for seven days (days 77-84). Blood samples were obtained from the eyes of the rats to assess the level of antioxidant enzymes before the treatment. On the last day of the treatment (day 84), the rats were sacrificed for blood sampling and measurement of antioxidant enzymes after the treatment.

Figure 1. Timeline Diagram of Experimental Protocol before and after Treatment (After matting on G12.5, a VPA rat model was developed; behavioral and antioxidant tests carried out before and after treatment)

Behavioral Assays

Evaluation of Social Interaction

Social interaction was evaluated using the method proposed by Hara et al. (23). In brief, the rat was individually familiarized with the trial cage for 60 minutes. Afterwards, another rat was introduced into the cage, and the face and anogenital sniffs (sniffing behaviors) of the first rat were evaluated for 20 minutes.

Evaluation of Repetitive Behavior

Repetitive behavior is an essential characteristic of ASD (24). The Y-shaped maze device is composed of Plexiglass and has three arms perpendicular to each other, each marked with letters A, B, and C. In this approach, repetitive behavior is measured by the Y-maze in a dark and quiet room, so that the animal would perceive the minimum stress during the test.

Based on the method proposed by Merali et al., we used the Y-maze to evaluate repetitive behavior (25). At the outset of the experiment, each rat (no prior familiarity with the device) was placed in the starting primary part of the arm (arm A) with the closed guillotine lid. After one minute, the guillotine lid was removed to begin the test. For 10 minutes, the arms that the animal entered were recorded. Spontaneous alternation was also considered as an indicator to assess repetitive behavior, and the reduction of spontaneous alternation behavior was regarded as a marker of elevated repetitive behavior. Spontaneous alternation behavior is demarcated with entry into the entire arms sequentially; for instance, if the animal makes arm entries sequentially as ABC, BCA, or CAB within 10 min. The following equation was used to calculate the percentage of alternation:

$$Spontaneous\ alternation\ = \frac{total\ number\ of\ arm\ alternations}{total\ number\ of\ arm\ entries - 2} \times\ 100$$

Antioxidant Enzyme Activity

SOD activity was measured using the method proposed Madesh and Balasubramanian using an ELISA reader at the wavelength 570 nanometers (26). CAT activity was also assayed based on its capability to decay hydrogen peroxide (H_2O_2) at the wavelength of 240 nanometers via spectrophotometry using the method proposed by Aebi (27). The reduction of GSH was measured at the wavelength of 412

nanometers using an ELISA reader via its response with 5, 5′-dithiobis using Ellman's technique (28).

Statistical Analysis

Data analysis was performed in Microsoft Excel 2013 (version 15.0) and Graphpad Prism 9 software. Two-way analysis of variance (ANOVA) was applied with six rats and five groups in each test (behavior, antioxidant enzymes). In addition, multiple comparisons were performed using Tukey's post-hoc test to determine the differences between the five group of naïve (n=6), control (n=6), risperidone (n=6), raw camel milk with risperidone (n=6), and pasteurized camel milk with risperidone (n=6). The obtained results were expressed as mean and standard error of mean (SEM), and the P-value of less than 0.05 was considered statistically significant.

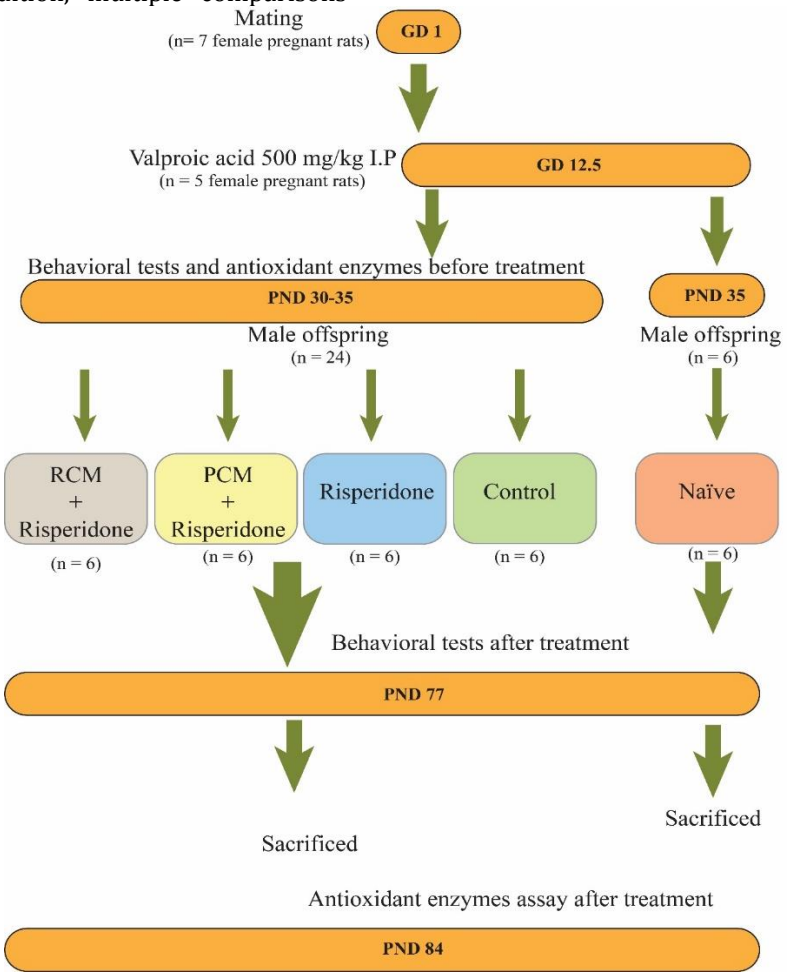

Figure 1. Time-line diagram showing the experimental protocol used before and after treatment. After matting in G12.5, we made a VPA-rat model, then behavior and antioxidant test accomplished before and after treatment.

Results

Effects of Camel Milk and Risperidone on the Repetitive Behavior of the Rats with Prenatal VPA Exposure

The effects of raw and pasteurized camel milk administered with risperidone were evaluated on social interaction impairment in the rats prenatally exposed to VPA (Figure 1-A). The results of two-way ANOVA showed a significant effect in spontaneous alternation behavior in the Y-maze test ($P<0.001$) (Figure 1). In addition, the post-hoc analysis indicated that the in-utero injection of VPA could significantly decrease the rate of spontaneous alternation behavior compared to the naïve group ($P<0.001$), ultimately revealing repetitive behavior. Nonetheless, the postnatal administration of

camel milk with risperidone reversed the rate of spontaneous alternation behavior after the treatment of VPA-induced diminution. Significant differences were also observed before and after the treatment between the raw milk with risperidone group and the pasteurized camel milk with risperidone group, respectively (P<0.01, P<0.001).

According to the findings, risperidone exerted no significant effects after the treatment. On the other hand, the administration of raw camel milk with risperidone (P<0.05) and pasteurized camel milk with risperidone (P<0.01) exerted significant effects compared to the control group after the treatment. The comparison of raw and pasteurized milk indicated that the latter had a more significant effect on VPA-induced autism in the rats (P<0.05).

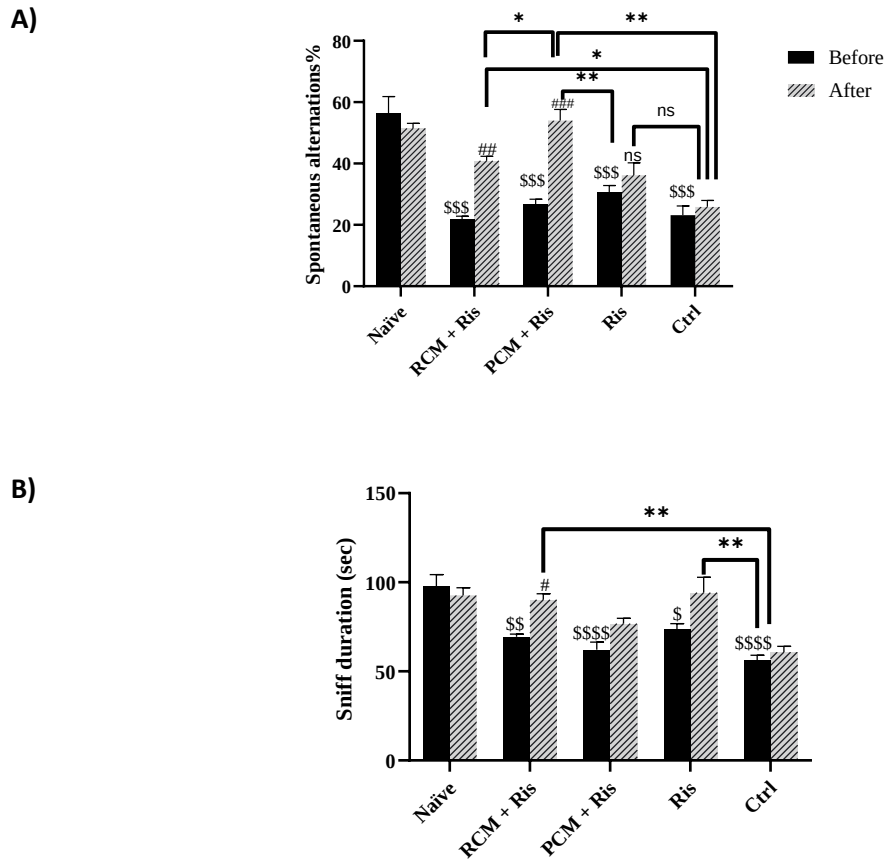

Figure 2. Effect of Risperidone (Ris), Raw camel milk (RCM), and Pasteurized camel milk (BCM) treatment on the percent of the spontaneous alternation in Y-maze (A) sniffing duration for social interaction (B). in autistic rats induced by VPA. The mean ± SEM (n = 6) showed for the data. Tukey's post hoc was used to compare among groups. (#) P<0.05 (##) P<0.01, (###) P<0.001 when compared before and after treatment, (*) P<0.05, (**) P<0.01 and (***) P<0.001 when compared among groups after treatment. ($) P<0.05 ($$) P<0.01, ($$$) P<0.001 P<0.05 when compared between naïve and other groups before treatment.

Effects of Camel Milk and Risperidone on the Social interaction of the Rats with Prenatal VPA Exposure

Social investigation (e.g., face and anogenital sniffing) is considered to be a crucial factor in the social interaction test of rats (23). In this study, we evaluated the social interaction of the rats prenatally exposed to VPA and determined the effects of risperidone and raw and pasteurized camel after 42 days of treatment using the sniffing duration test (Figure 2-B). The results of two-way ANOVA indicated a significant effect in all the groups with prenatal exposure to VPA compared to the naïve group before the treatment in the sniffing duration test (P<0.001). After 42 days of treatment, raw camel milk was observed to improve social interaction compared to before the treatment (P<0.05) and the control group (P<0.01).

However, no significant improvement was denoted in social interaction in the other groups compared to before the treatment. Moreover, a significant effect was observed in the risperidone group compared to the control group (Figure 2-B).

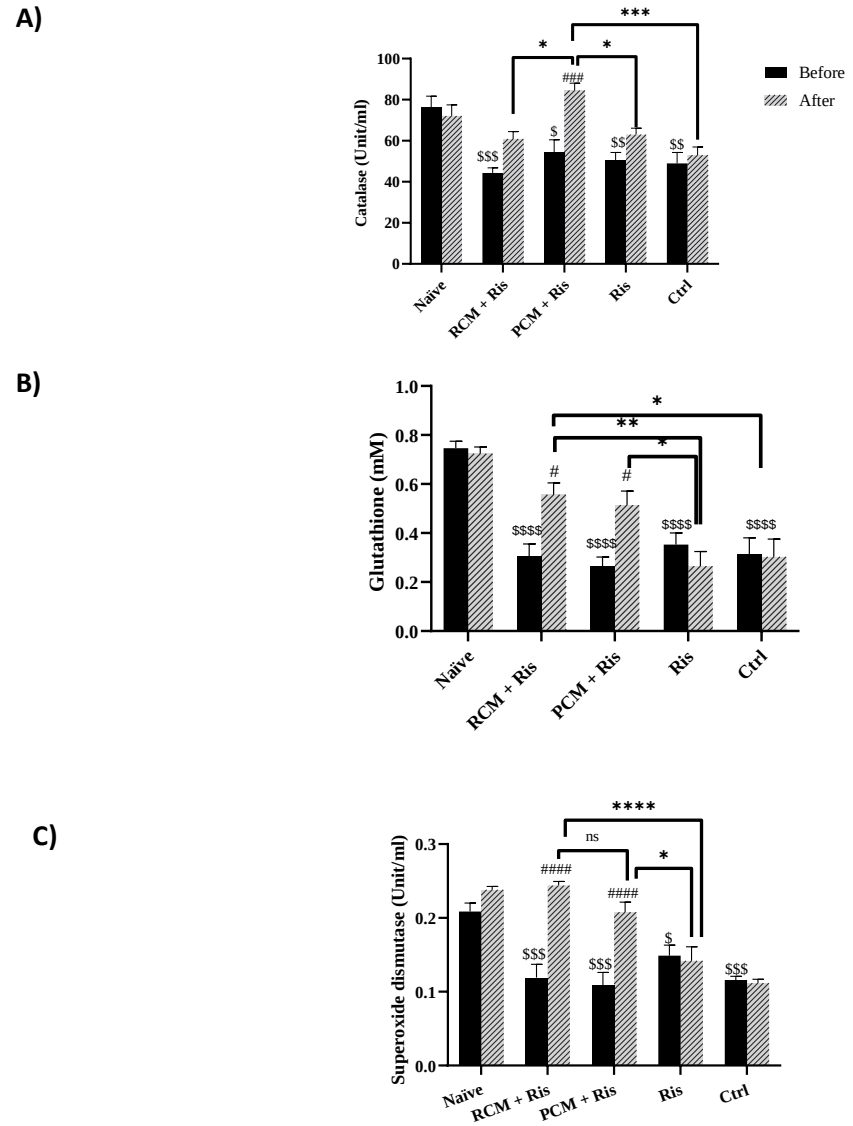

Figure 3. Effect of Risperidone (Ris), Raw camel milk (RCM), Pasteurized camel milk (PCM), and on catalase (CAT) (A), glutathione (GSH) (B), and superoxide dismutase (SOD) (C). in plasma level of autistic rats induced by Valproic acid (VPA). Values are shown as the mean ± SEM (n = 6). Tukey's post hoc was used to compare among groups. (#) P<0.05 (##) P<0.01, (###) P<0.001 when compared before and after treatment, (*) P<0.05, (**) P<0.01 and (***) P<0.001 when compared among groups after treatment. ($) P<0.05 ($$) P<0.01, ($$$) P<0.001 P<0.05 when compared between naïve and other groups before treatment.

Biochemical Tests

Effects of Camel Milk and Risperidone on the CAT Activity of the Rats with Prenatal VPA Exposure

Compared to the naïve group, the other groups with prenatal exposure to VPA had significantly lower CAT activity before the treatment (P<0.001, P<0.01, P<0.05). On the other hand, treatment with pasteurized camel milk and risperidone could significantly enhance CAT activity after the treatment (P<0.001). In addition, the co-administration of raw camel milk and risperidone exerted a significant effect compared to the control group (P<0.001). No significant effects were observed in the case of raw camel milk and risperidone administration

and risperidone treatment only (Figure 3-A), while a significant difference was denoted between raw and pasteurized camel milk in this regard (P<0.05).

Effects of Camel Milk and Risperidone on the GSH Level of the Rats with Prenatal VPA Exposure

On PND30-35, the GSH level of the rats with prenatal VPA exposure significantly reduced compared to the naïve group (P<0.001). However, treatment with camel milk (raw/pasteurized) and risperidone reversed the GSH level (P<0.05), and the GSH level was observed to be higher compared to the control group (P<0.05) (Figure 2-B). No significant difference was observed in the risperidone group in this regard after 42 days of treatment (Figure 3-A).

Effects of Camel Milk and Risperidone on the SOD Activity of the Rats with Prenatal VPA Exposure

The rats with prenatal VPA exospore had significantly lower SOD activity compared to the naïve group (P<0.0001, P<0.05). In addition, treatment with camel milk (raw/pasteurized) and risperidone significantly improved SOD activity compared to before the treatment (P<0.0001) and the control group (P<0.0001) (Figure 2-C). The comparison of camel milk and risperidone co-administration to risperidone alone indicated a significant difference between these treatments (P<0.05). Notably, risperidone could not improve the VPA-induced oxidant stress, and SOD activity was observed to decrease.

Discussion

The present study aimed to evaluate the effects of camel milk on two critical factors in autistic symptoms (i.e., repetitive behavior and impaired social interaction) and assess the antioxidant enzyme activity of rats with VPA-induced autism. According to the obtained results, prenatal exposure to VPA caused impairment in social interaction and repetitive behavior. In addition, prenatal VPA exposure increased oxidative stress due to the reduction of antioxidant enzymes. Nonetheless, behavioral autism and antioxidants were improved after 42 days of treatment with camel milk in the rats with VPA-induced autism.

In terms of psychological scales (e.g., CARS, SRS, ATEC, thymus, and TARC), previous findings have indicated that the daily consumption of camel milk could completely eliminate autistic behaviors in some patients. As for other patients, a partial decrease has been reported in the disease symptoms, overall indicating the beneficial effects of camel milk on the alleviation of autistic behaviors in autistic children (15, 21, 22, 29).

Repetitive behavior is considered to be a major symptom in autistic patients, which is often been associated with stress and defective social behaviors (5) and might be a consequence of communication problems (30). Previous findings in this regard have indicated decreased spontaneous alternation in rats exposed to VPA, representing increased repetitive behavior or functional memory deficits in the Y-maze test (31-33).

Repetitive behavior could be caused by the disruption of oxidative homeostasis through the activation of Wnt/β-catenin signaling pathway due to VPA induction. Furthermore, the deficiency of the GSH system in the frontal cortex has been associated with repetitive behavior in mice (7). In this regard, Mirza and Sharma recently reported that prenatal VPA exposure induced social impairment and repetitive behavior in the Y-maze test. On the other hand, treated rats with prenatal VPA exposure indicated higher oxidative stress levels, followed by increased thiobarbituric acid in reactive species and decreased GSH in the cerebellum, brainstem, and prefrontal cortex (7).

In another study, Kumar et al. stated that pre-VPA treatment could significantly decrease the rate of spontaneous alteration compared to naïve animals in the Y-maze test, which is indicative of increased repetitive behavior (34). Moreover, a recent study indicated that in-utero VPA significantly increased repetitive behavior in the Y-maze test (33). In this regard, our findings showed that the rate of spontaneous alteration significantly reduced in the rats with prenatal VPA exposure, which proposed repetitive behavior in these animals. Furthermore, camel milk and risperidone could improve repetitive behavior in the VPA-exposed rats. Notably, pasteurized camel milk had a more significant effect compared to raw camel milk (Figure 2-A).

In a study conducted by Al-Amin et al. (2015), VPA-exposed offspring had low social interaction based on the measured number of sniffing. Poor social behavior could be caused by

fear, anxiety, and impaired understanding of communicational signals from stranger mice. In the mentioned study, astaxanthin was administered to improve the impaired social interaction in the animals prenatally exposed to VPA (35). In another research by Hara et al., Tukey's post-hoc multiple comparison test indicated that sniffing duration in VPA-exposed mice significantly decreased, and treatment with risperidone significantly alleviated social interaction by increasing the sniffing duration (36). Our findings in this regard are consistent with the mentioned study as the sniffing duration reduced in the rats with prenatal VPA exposure. In addition, the co-administration of camel milk and risperidone could improve the social defects in these rats, while raw camel milk was observed to be more effective (Figure 1-B).

According to the literature, embryonic exposure to VPA increases the risk of autism in children. In the present study, VPA regulated gene expression through chromatin remodeling via hindering the histone deacetylase (HDAC) activity on GD12.5, which was followed by the manifestation of autistic behavioral phenotypes (37). Notably, alpha-lactalbumin in milk regulates HDAC via the NF-κB pathway (38).

Another study in this regard showed severe deficiency in the GABAergic function of patients with ASD and other ASD models (39). Furthermore, a recent study indicated that oligofructose dietary intake through milk could alleviate cognitive performance and affect olfactory bulb structural progress and hippocampal gene expression through the regulation of GABAergic and chromatin remodeling processes (40). Another research also demonstrated that fluoxetine (Prozac), which is extensively used for the treatment of mood disorders, added to milk during lactation interfered with GABAergic transmission (41). Another study showed that fatty acids (C6-C18) in maternal milk could decrease anxiety through the regulation of GABAergic neurotransmission in rats (42). As previously reported, camel milk could regulate GABA activity by exerting neuromodulatory effects on dopamine and serotonin; notably, it is considered to be negative regulator of dopamine (29).

All plant, animal, and human cells produce antioxidant enzymes (e.g., SOD, CAT, GSH) to strengthen a ubiquitous antioxidant enzyme system for defense against oxidative stress. In the current research, VPA treatment significantly reduced antioxidant enzymes (CAT, SOD, and GSH). Several studies have confirmed that autistic patients have defective oxidative stress, and VPA-induced autism may be responsible for oxidative stress (9, 13, 33, 43, 44).

According to the results of the present study, the co-administration of risperidone and camel milk significantly increased the antioxidant enzyme activity of CAT, SOD, and GSH in the rats with VPA exposure compared to before the treatment (Figure 2). Previous findings have also indicated that camel milk could alleviate the neurotoxic damage induced by fenpropathrin in the brains of rats through the regulation of oxidative stress (45). Moreover, the peptide drove of the caseins in camel milk have exhibited antioxidant properties (46).

VPA causes deficits in the antioxidant system and affects the hippocampus and prefrontal cortex, thereby increasing oxidative stress. In the current research, the exposure of the rats to VPA significantly decreased CAT, GSH, and SOD activity in the prefrontal cortex and hippocampus of the exposed rats compared to the naïve group (33). Furthermore, prenatal VPA exposure increased nitrite and malondialdehyde levels due to deficiency in the antioxidant system in the hippocampus and prefrontal cortex. However, the in-utero exposure of the rats to VPA significantly diminished CAT, GSH, and SOD activity in the prefrontal cortex and hippocampus compared to the naïve group (33). Therefore, it was concluded that after the induction of autism by VPA in the rats, the enzyme activity of CAT, GSH, and SOD reduced (Figure 2), possibly inducing oxidative stress via VPA injection.

Several studies have confirmed improved autistic symptoms by using antioxidant supplements (e.g., zinc, magnesium, vitamins E and C). These compounds are essential to antioxidant enzyme activity, GSH synthesis, and absorption of antioxidant vitamins. Therefore, they also play a pivotal role in the improvement of oxidative stress. (15, 47). Evidence suggests that camel milk contains numerous antioxidant nutrients, such as zinc, magnesium, vitamin E, vitamin C, and copper (47).

CAT has an important function against ROS by converting H_2O_2 into water. In several reports, the activity of CAT has been reported to

decrease following VPA exposure in autistic patients. Researchers have previously used various treatments to increase CAT activity (4, 13, 15, 35). After treatment with VPA in the present study, the enzyme activity of CAT was observed to decrease. After the treatment period with camel milk, CAT activity could be enhanced as well (Figure 2-A). Notably, the pasteurization of camel milk was observed to further improve CAT activity (e.g., repetitive behavior) compared to raw camel milk.

According to a study in this regard, camel milk significantly improved the antioxidant capacity of the brain in terms of VPA-induced autistic behavior. GSH is an intracellular antioxidant that maintains the reductive state of the intracellular microenvironment and decreases oxidative stress by its neuroprotective properties. Patients with ASD often present with the deficiency of the GSH redox metabolism pathways due to an inefficient detoxification system (15). In the mentioned study, the GSH level significantly decreased in the treated rats compared to the naïve group (13, 15), indicating the defective defense mechanisms against ROS.

The results of the present study showed a significant increase in the GSH level after treatment with camel milk, which could be attributed to the antioxidant nutrient content of camel milk (Figure 2-B). As mentioned earlier, camel milk contains various antioxidant nutrients, such as zinc and magnesium. Therefore, the antioxidant properties of camel milk are induced through the effects of magnesium on the reduction of oxidative stress and stimulation of vitamin E and C absorption, while zinc elevates total GSH and SOD levels (29).

SOD plays a key role in the inhibition of lipid peroxidation through the decomposition of superoxide into hydrogen peroxide and oxygen. On the other hand, deficient SOD activity and accumulated superoxide cause toxicity. Several studies have shown the significant reduction of SOD activity in autistic children in humans or VPA-induced autism in rats (13, 15). In addition, low SOD level could arise from the nutritional amount; for instance, low copper reduces SOD, while low zinc decreases SOD and other antioxidant compounds (29). In the current research, SOD activity significantly increased after treatment with camel milk, which could be attributed to the high content of zinc, magnesium, copper, and vitamin E in camel milk (Figure 2-C).

A recent study demonstrated that exosomal kappa casein and lactoferrin in camel milk could effectively enhance the oxidative stress induced by cyclophosphamide in rats (46). However, risperidone has been reported to have fewer antioxidant properties (48), while another research indicated that risperidone could reduce GSH and SOD activity in the cortex and hippocampus of rats perinatally treated with perinatal phencyclidine (49). However, risperidone caused no significant changes in the antioxidant activity after 42 days of treatment in the present study.

Conclusion

According to the results, camel milk caused VPA-induced impairment in the social interaction and repetitive behavior of the autistic rats through the improvement of the antioxidant defense system.

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