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Abstract: Energy drinks enhance physical endurance and cognitive ability. The ingredients present in these drinks are considered as ergogenic and have memory boosting effects. In the present study effects of taurine administration for one week was monitored on physical exercise and memory performance in rats. Animals were divided into two groups namely control and test. Taurine was injected intraperitoneally to the test group at the dose of 100mg/kg. After one week of treatment rats were subjected to physical exercise and memory task. Results of this study revealed that rats injected with taurine for one week exhibited improved muscular strength as well as enhanced memory performance in Morris water maze and elevated plus maze. Biomarker of lipid peroxidation was significantly reduced in brain and plasma of test animals. Taurine administration also resulted in higher levels of corticosterone in this study. The results highlight the significance of taurine ingestion in energy demanding and challenging situations in athletes and young subjects.

Keywords: Memory function, oxidative stress, physical endurance, taurine.

INTRODUCTION

Energy drinks are the most widely used beverages especially among youngsters and athletes. Mostly these drinks are used to boost physical energy, stimulate mood and to elevate muscular endurance. The ingredients which make the energy drink as energy-boosting beverage includes caffeine, guarana, ginseng, and taurine (Higgins *et al*., 2010). Taurine is a naturally occurring non-protein amino acid found in most tissues of animals including humans. It is essential for skeletal muscle and development and function of cardiovascular system (Schuller-Levis and Georgia 2003). It is suggested that supplementation of taurine may increase uptake of taurine which may lead to increase in skeletal muscle contraction in athletes (Imagawa *et al*., 2009). Muscular contraction is an important factor for the performance of an athlete. Previously, taurine containing drink is reported to improve physical endurance in athletes (Kim *et al*., 2016). There are studies which have represented the antioxidant ability of taurine. Oliveria *et al*., in 2010 showed that *in vitro* taurine treatment prevented hydroperoxide-induced damages in rat liver slices by reducing oxidative stress. It has been observed that taurine deficiency reduces the expression of mitochondrial-encoded proteins and thus increases the production of free radicals due to reduced activity of electron transport chain (Schaffer *et al*., 2009). Thus it can be hypothesized that sufficient taurine content in muscle can reduce oxidative stress during excessive muscular activity.

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Consumption of energy drinks showed to increase memory performance and mental alertness in human subjects (Alford *et al*., 2001). Studies showed the enhancement of cognitive ability and mood following the intake of energy drinks suggested the involvement of caffeine, glucose and taurine (Giles *et al*., 2012). Likewise drinks that contain the combination of caffeine and taurine attenuated fatigue and improved psychomotor behavior (Howard and Marczinski, 2010). Taurine is concentrated in brain stem and hippocampus (Gebara *et al*., 2015) where it acts as neuromodulator, neuroprotector, membrane stabilizer and regulates cellular calcium levels (Wu and Prentice, 2010). Previous studies suggest that taurine administration protects neurotoxicity-induced learning and memory deficits and enhances long-term potentiation (Chepkova *et al*., 2006). Since brain is a highly active organ, therefore, oxidative stress is a normal phenomenon in neuronal cells (Massaad, 2011). Use of antioxidant rich diet is beneficial to improve brain activity. Scavenging the free radicals or increasing the antioxidant enzyme activity results in enhanced neuronal function (Bhatti *et al*., 2016). Dietary supplementation of antioxidant has been shown to cross blood-brain barrier, increase synaptic plasticity and improve hippocampus-dependent memory in mice (van Praag *et al*., 2007). There is accumulating data suggesting the use of antioxidant nutrients to reduce the onset of dementia and cognitive decline (Otsuka, 2016). Taurine having antioxidant ability is suggested to improve neuronal activity and thus may enhance cognitive function.

Glucocorticoid is another important factor for the physical and mental activities (Sünram-Lea *et al*., 2012). Under physical and demanding conditions the level of cortisol also varies. Cortisol is the hormone which is associated with stress and physically active situations (Ranabir and Reetu, 2011). The degree of increased glucocorticoid determines its effects on memory performance. Acute and moderate increase in cortisol levels is related to increased memory function whereas chronic and continuous release causes memory impairment (Yuen *et al*., 2011; Schutsky *et al*., 2011). Taking into account of this literature background the present study was, therefore, designed to examine the effects of taurine administration on the muscular strength of rats during exercise and their performance in memory testing activity. The role of glucocorticoid and antioxidant status was also investigated to suggest the possible mechanism behind these behavioral aspects following the administration of taurine for one week.

MATERIALS AND METHODS

Animals

12 locally bred Albino Wister rats (200-250g) purchased from Dow University Ojha Campus were used in the study. All animals were housed individually under a 12h light-dark cycle (light on at 6:00h) and controlled room temperature (22+2)°C with free access to cubes of standard rodent diet and tap water for at least 3-4 days before experimentation. All experiments were conducted according to a protocol approved by Local Animal care Committee performed in line with National Institute of Health Guide for Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985).

Experimental protocol

Animals were randomly divided into control and test groups (n=6). Controls were injected with saline (0.9%) and test groups were injected with taurine (100mg/kg). Behavioral activity of rats was monitored after one week of treatment. Rats were subjected to pole test, weight test and Kondziela inverted screen test to evaluate physical endurance. Whereas, Morris water maze (MWM) and elevated plus maze (EPM) were used to analyze memory retention following one week administration of taurine in rats. Immediately, after behavioral analysis rats were decapitated to collect the plasma and brain sample and stored at -70^{o}C. Plasma and brain samples were used to estimate malondialdehyde levels (MDA), catalase activity and corticosterone levels.

Behavioral test

Pole test

A pole test was performed as a way of evaluating bradykinesia in rats. In brief, rats were placed head-up on top of a vertical wooden pole (2.5cm in diameter and 100 cm in height) and base of the pole was placed in the home cage filled with sawdust. When placed on the pole, animals orient themselves downward into their home cage. The time to descend (sec) from the top of a rough-surfaced pole to the floor was recorded in rats (Yanpallewar *et al*., 2004).

Kondziela inverted screen test

Kondziela inverted screen test has been used previously for measure of muscular strength of animals using all four limbs (Madiha *et al*., 2017). The inverted screen is a 43 cm square of wire mesh consisting of 12mm squares of 1 mm diameter wire. It is bordered by a 4cm deep wooden beading (which prevents animals from climbing on to the other side). The test was done by placing the rat in the centre of wire mesh screen which was rotated to an inverted position over 120 seconds with the rats head declining first. The time when the rat fell off from the screen was noted.

Weight test

In weight test ball of tangled fine gauge stainless steel wires with different weights were used. The weights consisted of 20g, 30g, 45g, 65g and 98g links. During this test each rat was held from the middle of tail and allowed it to hold the weight from its forepaws. Weights were used in increasing order. If rat successfully grasped the weight then the next heaviest weight was used to analyze the muscular strength. Total cut off time for each weight was 3 sec. A final total score was calculated as the product of number of links in the heaviest chain hold for 3 sec, multiplied by the time (sec) it was held.

Memory assessment

The dimensions of the apparatus used for MWM and EPM their procedures were same as described earlier (Haider *et al*. 2015a). In this experiment memory retention was observed after 24 h of training session.

Oxidative parameters

The whole brains were removed, rinsed in isotonic saline, and weighed. A 10% (w/v) tissue homogenate was prepared with 0.1M phosphate buffer (pH 7.4) and centrifuged at 10,000×g for 10min at 4◦C. The supernatant was used for the estimation of lipid peroxidation (Chow and Tappel 1971) and catalase (Sinha 1972) activity.

Plasma corticosterone levels

The procedure for the estimation of plasma corticosterone was same as mentioned earlier (Haider *et al*., 2013)

STATISTICAL ANALYSIS

Results are presented as means ±S.D (n=6). Data of pole test, MWM, EPM, MDA and catalase activity were analyzed by independent sample *t*-test via SPSS version 20.0 software. Whereas, Mann–Whitney *U*-tests was used to statistically analyze weight test score and Kondziela

inverted screen score. *p* values <0.05 were considered significant.

RESULTS

Physical endurance

Pole test

Data for pole test was performed by independent sample *t*-test (fig. 1). It was revealed that taurine administration for one week significantly increased [$t(10)$ =3.207, $p<0.01$] time to descend the pole in test animals (11±3.39 sec) as compared to control rats (4.5±1.8 sec).

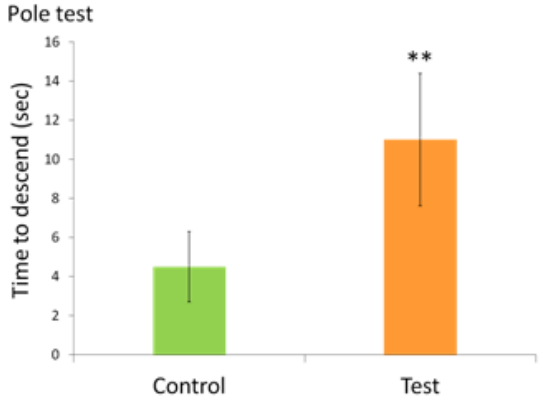

Fig. 1: Effects of one week taurine administration on pole test activity. Data is represented as mean±SD (n=6). Significant difference was obtained by independent sample *t*-test. **$p<0.01$ as compared to controls.

Kondziela inverted screen test

Data for Kondziela inverted screen scores was also analyzed by Mann-Whitney *U*-test (fig. 2). Test animals (18±2.2) showed significantly ($p<0.01$) higher inverted screen score as compared to controls (10.66±1.2).

Weight test

Data for weight test scores was analyzed by Mann-Whitney *U*-test (fig. 3). Test animals (12±2.44) showed significantly ($p<0.01$) higher weight score as compared to controls (7±1.89).

Memory testing

Morris water maze (MWM)

MWM was performed to evaluate the effects of taurine administration on spatial memory (fig. 4). Data was analyzed by independent sample *t*-test and it was observed that escape latency was significantly decreased [$t(10)$ =5.67, $p<0.01$] in test group (7±0.8 sec) as compared to controls (16±3.8 sec) indicating 7 days of taurine administration at the dose of 100mg/kg increases memory functions.

Elevated plus maze (EPM)

Memory function was also monitored by EPM in terms of transfer latency (fig. 5). Independent sample *t*-test showed significant memory retention [$t(10)$ =16.32, $p<0.01$] in test group following administration of taurine at the dose of 100 mg/kg for one week. Taurine administrated rats (32±5.5 sec) took lesser to enter into the save area of EPM as compared to controls (120±12 sec) during test session.

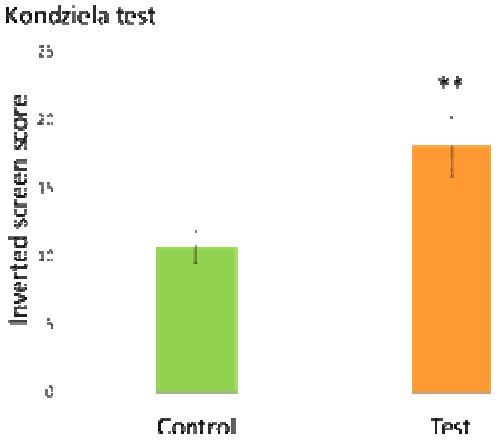

Fig. 2: Kondziela inverted screen test was performed to evaluate muscular activity. Values are mean±SD (n=6). Significant difference was obtained by Mann–Whitney *U*-tests. **$p<0.01$ as compared to controls.

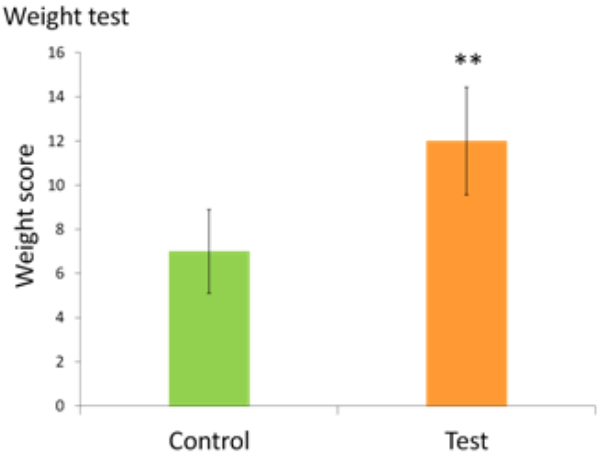

Fig. 3: Muscular strength was also monitored by weight test. Values are mean±SD (n=6). Significant difference was obtained by Mann–Whitney *U*-tests. **$p<0.01$ as compared to control animals.

MDA levels

MDA level in rat brains was determined as a biomarker of lipid peroxidation. fig. 6 describes the levels of MDA in the brain of control and test groups. Analysis by Student's t-test revealed that 15 days of taurine administration at the dose of 100 mg/kg/ml significantly decreased [$t(10)$ = 7.94, $p<0.01$]. MDA levels in test rats (43.15+7.37 µmol/g) as compared to controls (67.3+1.05µmol/g). MDA levels in plasma was also significantly decreased [$t(10)$ = 4.15, $p<0.01$] in test rats (16.41±2.16µmol/g) as compared to controls (25.97±2.16 µmol/g).

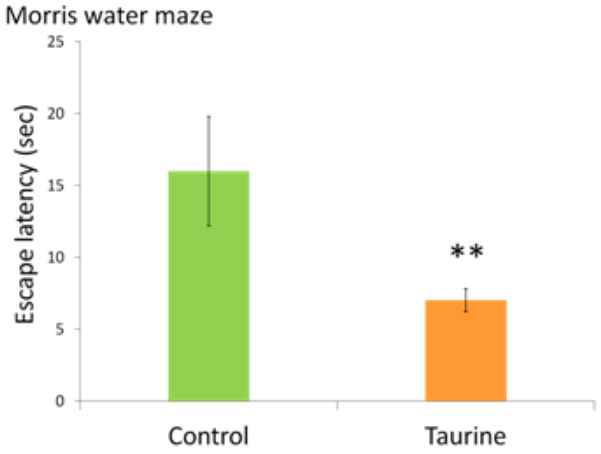

Fig. 4: Effects of one week taurine administration on Morris water maze activity. Values are mean±SD (n=6). Significant difference was obtained by independent sample *t*-test. ***p*<0.01 as compared to controls.

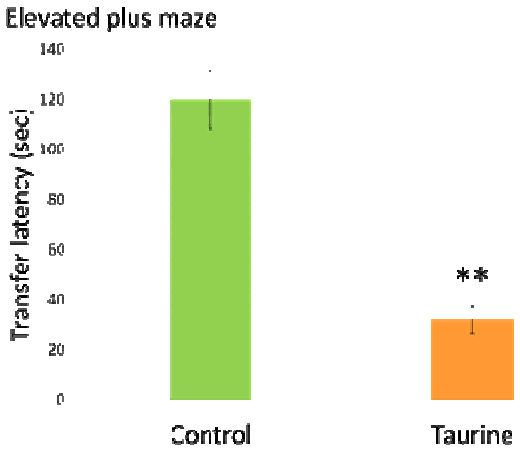

Fig. 5: Memory function was also observed by elevated plus maze following the administration of taurine. Data is represented as mean±SD (n=6). Significant difference was obtained by independent sample *t*-test. ***p*<0.01 as compared to controls.

Catalase activity

Fig. 7 shows brain CAT activity following the administration of taurine for 15 days. Student's t-test revealed significant decreased [$t(10) = 7.85$, $p<0.01$] CAT activity in test groups (58.74+2.16 µmol/min/g) as compared to controls (74.42±4.39 µmol/min/g). Catalase activity in plasma was also significantly decreased [$t(10) = 6.64$, $p<0.01$] in test groups (56.39±7.9 µmol/min/g) as compared to controls (85.39±7.15µmol/min/g).

Plasma corticosterone levels

Corticosterone levels in plasma (fig. 8) was significantly increased [$t(10) = 3.211$, $p<0.01$] in test groups (0.576±0.017µg/ml) as compared to controls (0.695±0.089µg/ml).

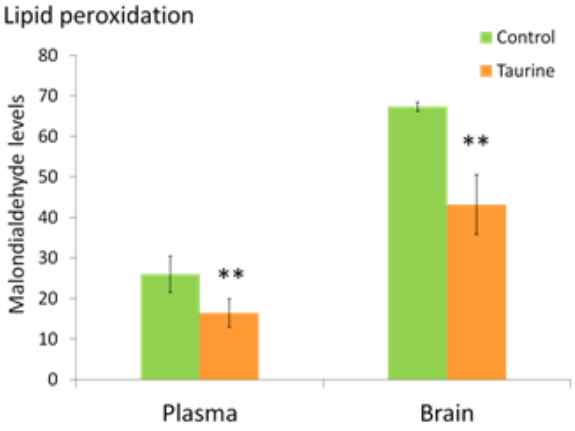

Fig. 6: Lipid peroxidation was estimated in terms of malondialdehyde levels in plasma (µmol/ml) and brain (µmol/g) of control and test animals. Data is represented as mean±SD (n=6). Significant difference was obtained by independent sample *t*-test. ***p*<0.01 as compared to control values.

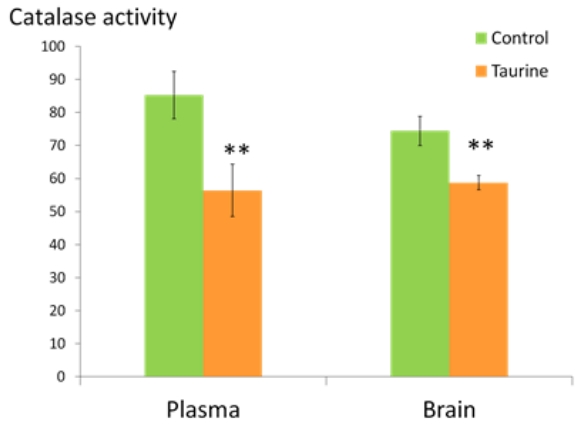

Fig. 7: Effects of taurine administration on catalase activity in plasma (µmol/ml/min) and brain (µmol/g/min). Data is represented as mean±SD (n=6). Significant difference was obtained by independent sample *t*-test. ***p*<0.01 as compared to control values.

DISCUSSION

Energy drinks are widely used by people to enhance performance in sports and in challenging situations. Taurine and caffeine containing drinks showed to enhance physical endurance, mental performance and mood in human subjects (Alford *et al*., 2001). This study was conducted to evaluate the effects of sub-acute administration of taurine on physical activity during physical exercise and memory performance in rats. In the present study pole test, weight test and Kondziela inverted screen test were used to monitor physical activity of rats following the administration of taurine. These tests are conventionally used to evaluate the muscular strength of rodents using all four limbs. Results showed that the rats

treated with 100mg/kg taurine for one week exhibited increased muscular strength as evident by increased time to descend, weight score and time of falling in pole test, weight test and Kondziela inverted screen test, respectively. This study is consistent with the previous study reported by Miyazaki and co-workers in 2004. The increased muscle taurine and muscle contraction has also been shown following the supplementation of taurine in rodents (Spriet and Whitfield 2015). Our results also showed memory enhancing effects of taurine treatment. Rats treated with taurine showed improved memory retention in MWM and EPM task. Increased alertness and better cognition has been associated with the intake of energy drinks (Childs, 2014). The composition of energy drinks is considered to be responsible for these behavioral effects. Glucose and caffeine rich drink previously showed enhanced cognitive ability (Sünram-Lea *et al*., 2012). Moreover, a combination of taurine and caffeine containing drink also showed positive effects on mental performance and mood in humans (Seidl *et al*., 2000). In this study one week administration of taurine in rats improved memory performance indicating taurine content of energy drink may also have significant memory enhancing effects.

The observed behavioral effects of taurine administration in the present study are concomitant with decreased oxidative stress biomarker. MDA levels and catalase activity were significantly decreased in both plasma and brain samples. Antioxidant property of taurine has been reported previously (Cozzi *et al*., 1995). It is suggested that taurine is not the free radical scavenger. Jong *et al* in 2012 investigated the mechanism of antioxidant property of taurine and they showed that inhibition of taurine results in inhibition of aconitase enzyme, cessation of mitochondrial electron transport chain (ETC) and reduced oxidation of glutathione. The inhibition of ETC causes the diversion of electrons from ETC resulting in the formation of superoxide anions. The antioxidant enzymes are responsible for the removal of free radicals including superoxide anions (Lobo *et al*., 2010). Superoxide dismutase converts OH- radical into hydrogen peroxide (H_2O_2) which is then neutralized by catalase and glutathione peroxidase (Haider *et al*., 2015a). It has been shown that if enzyme is functioning properly then accumulation of free radicals may lead to increased activity of antioxidant enzymes and vice versa (Rahman, 2007). In the present study catalase activity was significantly reduced following the treatment of taurine suggesting the enhanced activity of respiratory chain which may have led to decreased production of free radicals, reduced catalase activity and thus resulted in decrease in MDA levels in plasma and brain.

Oxidative stress is considered as a detrimental factor to induce muscle fatigue and muscle atrophy (Cases *et al*., 2017). Free radicals cause the oxidation of Ca^{++} channel and affect Ca^{++} release from sarcoplasmic reticulum resulting in reduced muscular contraction (Steinbacher and Eckl, 2015). In this study increased availability of taurine reduced oxidative stress which may have increased Ca++ ions in muscle cells, reducing muscle fatigue and hence increased muscular activity during pole test, weight test and Kondziela inverted screen test. Likewise, the role of oxidative stress is also well reported in memory formation. Oxidative stress induces excitotoxicity, increases generation of free radicals and alters synaptic functions which are associated with cognitive decline in neurodegenerative diseases (Salim, 2017). Reduction in free radicals and oxidants leads to reduced oxidation of lipid bilayer, increased membrane signaling and synaptic plasticity (Ding *et al*., 2017). In the present study improved memory performance in taurine treated rats may be attributed to the reduced oxidative stress in brain.

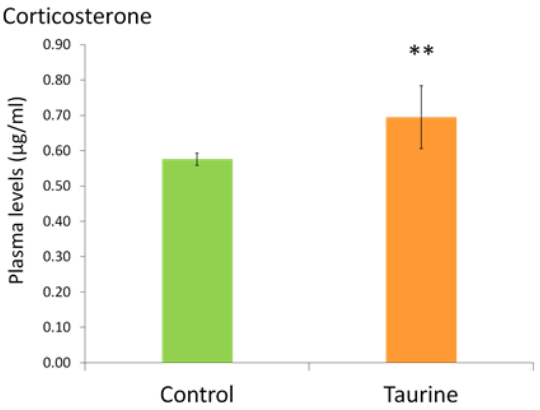

Fig. 8: Plasma corticosterone levels in plasma (µg/ml) of control and test animals following the administration of taurine. Data is represented as mean ± SD (n=6). Significant difference was obtained by independent sample *t*-test. ***p*<0.01 as compared to control values.

Plasma corticosterone were also measured following the administration of taurine with the idea that energy drinks may enhance hypothalamic pituitary adrenal (HPA) axis resulting in increased glucocorticoid levels (García *et al*., 2016). The involvement of glucocorticoid in increased physical activity has been reported earlier (Du *et al*., 2017). This steroid hormone has catabolic nature. It enhances the glucose levels under energy demanding situations (Kuo *et al*., 2015). In this study the increased corticosterone levels by taurine treatment may also be accountable for increased muscular endurance by providing glucose during energy demanding physical exercise (Sylow *et al*., 2017). Moreover, moderate increase in glucocorticoid is useful for improved memory performance, alertness and brain active state (de Kloet *et al*., 2005). Acute stress-induced increased corticosteroids and enhanced memory function is extensively reported (Haider *et al*., 2015b). Corticosteroids influence excitatory synaptic transmission and synaptic plasticity in

hippocampus (Joëls, 2008). It has been reported that acute stress-induced activation of glucocorticoid receptors enhances the functioning of glutamatergic receptors (Sylow *et al*., 2011). It has also been shown earlier that the enhanced glutamatergic function has direct impact on memory specific areas of brain and enhances working memory (Lisman *et al*., 1998). Previously, taurine administration showed to enhance glutamatergic release (El Idrissi and L'Amoreaux, 2008). Therefore, it can be suggested here that taurine-induced increased corticosterone causes an increase in glutamatergic neurotransmission and thus results in increase in memory performance in MWM and EPM task. This is the first study demonstrating increased corticosterone levels following the administration of taurine. The underlying mechanism is not yet known, however, caffeine which is one of the ingredients of energy drinks has also been demonstrated to increase glucocorticoid levels. Caffeine administration increases adrenocorticotropic hormone and cortisol in humans (Wu, 2015). It is noteworthy that taurine and caffeine both are increasing corticosteroids, the use of energy drinks therefore, should be limited as long-term increase in glucocorticoid may exert deleterious effects on health (Tatomir *et al*., 2014). However, we can suggest that the use of these ingredients of energy drinks may be useful and helpful to improve physical endurance and brain activity.

CONCLUSION

Taurine which is one of the important ingredients of energy drinks can be suggested for the improved activity of muscle during exercise for the individuals involve in energy demanding satiations such as athletes. Moreover, the present study emphasizes on the use of taurine to enhance mental performance. These effects of taurine may at least be in part due to its antioxidant ability and HPA-axis stimulating effects. This study also highlights that the use of taurine in different ailments may provide another field of research interest for future studies.

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