Future Natural Products
doi: 10.34172/fnp.2022.02 2022;8(1):2-6 http://futurenatprod.skums.ac.ir

Original Article

Anethole exerted anticonvulsant effect in pentylenetetrazole-model of seizure in male mice: Possible antioxidant effects

Sanaz Salimian[1], Saeid Habibian-Dehkordi[1*], Jahangir Kaboutari[1], Hossein Amini-Khoei[2], Mohammad Sajad Barkhordari[1]

[1]Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
[2]Medical Plants Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran

Abstract

Background and aims: Epilepsy is a neurological disorder causing brain dysfunctions. Treatment and control of epilepsy have long been a challenge in medical sciences. Despite the variety of current anticonvulsant drugs, research continues to discover new drugs with the highest efficacy and the lowest side effects. In the present study, the anticonvulsant effects of anethole in the seizure induction with pentylenetetrazole (PTZ) were evaluated in a mice model with respect to its possible antioxidant effects. PTZ is known to cause generalized epilepsy in animal models.

Methods: Accordingly, in this experimental study, 40 mice were divided into 5 groups; the first group received normal saline, the second group received 10 mg/kg diazepam, and the third to fifth groups were given anethole at 31.25, 62.5 and 125 mg/kg, respectively. Injections were conducted intraperitoneally for one week; then seizures were induced by the intravenous injection of 90 mg/kg PTZ. After determination of the duration of seizures in different groups, the mice were finally placed under deep anesthesia and their prefrontal cortex tissue was isolated to measure nitric oxide (NO), antioxidant capacity and malondialdehyde (MDA) concentrations.

Results: The results showed that anethole increased the delay in the onset of seizures, decreased the amount of nitrite in the brain, enhanced antioxidant capacity, and reduced MDA content in a dose-dependent manner.

Conclusion: Overall, our results indicated the anticonvulsant effects of anethole that could be mediated by inhibiting oxidative stress.

Keywords: Seizure, Mouse, Pentylenetetrazole, Anethole.

***Corresponding Author:**
Saeid Habibian-Dehkordi, Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran.
Tel: +98-38-32324427,
Email: habibian_dehkordi@yahoo.com

Received: 1 January 2022
Accepted: 28 February 2022
ePublished: 30 June 2022

Introduction

Seizure is a neurological disorder in which limited or wide areas of the brain have spontaneous activities and brain functions are impaired. Seizure is the second leading cause of neurological diseases after strokes (1). This neurological failure is severe, sudden and debilitating. About 1.6% of all age groups of the world's population are affected by the condition (2). Clinically, seizures are divided into two general and focal types. The most common type of seizure is its general type, and its symptoms include loss of consciousness and contraction of the tonic and colonic muscles. It usually lasts from 30 seconds to 3 minutes followed by a full recovery (3). In the focal type of seizure, abnormal motor and sensory behaviors can be seen, but consciousness remains unchanged (2,3).

Oxidative stress is caused by the release of free radicals in the brain. They can play a role in the onset and progression of epilepsy, although antioxidants such as vitamin E and glutathione can prevent the spread of seizures (4,5). Oxidative stress causes the formation of reactive oxygen species and reactive nitrogen species, triggering many harmful mechanisms such as inhibition of mitochondrial function, increased calcium levels and enhanced lipid peroxidation (6). Nitric oxide (NO) is a neurotransmitter regulator produced by NO synthase (NOS) from L-arginine (7). It is known that NO is involved in the pathophysiology of seizure (8). It has also been found that many drugs in animal models cause anticonvulsant effects by inhibiting NOS (9).

According to the previous researches, medicinal plants and their active ingredients, with fewer side effects, can be used as adjuvant drugs or very suitable alternatives for the treatment of this disease (10). Therefore, we focused on the effects of anethole in the present study.

Anethole (1-methoxy-4-isopropyl) is a colorless and sweet terpenoid; this ingredient, which has the same flavor as fennel, is 10 times sweeter than sugar (11,12). Relaxant and antispasmodic properties, and anti-inflammatory, anticancer and analgesic qualities have been reported for this compound (13-15).

The aim of the present study was to evaluate the anticonvulsant effect of anethole in a pentylenetetrazole (PTZ)-model of seizure in male mice with respect to its possible effects on oxidative stress.

Materials and Methods

Animals

In this study, 40 NMRI male mice weighing 25-30 g and approximately aged 8-12 weeks were used. The mice were kept in a room under standard light and temperature conditions; they had free access to appropriate food and water. The present study was conducted as per the Guide for the Care and Use of Laboratory Animals (8th edition, National Academies Press) as adopted by the Committee on the Care and Use of Laboratory Animals of Shahrekord University. All efforts were made to ensure the least use of animals and improve their well-being.

Study design

The mice were randomly divided into 5 groups (n=8) as follows; the first group received normal saline and the second group was given diazepam at 10 mg/kg. The third to fifth groups were given anethole at 31.25, 62.5 and 125 mg/kg, respectively (16). In all groups, agents were injected intraperitoneally for one week, and then PTZ was injected intravenously to induce seizure.

Determination of seizure threshold

In order to determine the seizure threshold in mice, we performed a previously described procedure.

Briefly, a winged infusion set (30 gauge) was used to infuse PTZ (0.5%) at a constant rate of 1 ml/min into the tail vein of the freely moving subject. The infusion was stopped whenever forelimb clonus followed by the full clonus of the body (began with running and then loss of righting reflex) occurred. The minimal dose of PTZ (mg/kg body weight) needed to induce a clonic seizure was considered as the index of seizure threshold. Because PTZ was administrated at a constant rate (1 ml/min), the duration to induce seizure depended on the dose and time of PTZ injection (17).

Measurement of total antioxidant capacity

Animals were euthanized under deep anesthesia and then prefrontal cortex was removed. Total antioxidant capacity (TAC) was then determined using the FRAP (ferric reducing ability of plasma) method at 37°C and pH 3.6, according to a previously described procedure (18). Absorbance was measured after 30 minutes and reported in proportion to the combined ferric reducing/antioxidant power of the antioxidants in protein. The results were expressed as mmol Fe^{2+}/mg protein.

Measurement of malondialdehyde

The malondialdehyde (MDA) level of the prefrontal cortex was measured according to a previously described method (19). By using thiobarbituric acid (TBA) and the method based on the development of colorful chromophores, following the reaction of TBA with MDA, the concentration of MDA was determined. Finally, the absorbance of the supernatants was measured at 562 nm for the prefrontal cortex specimens using ELISA reader.

Nitrite assay

The Griess reaction was run to measure nitrite, as described previously. To describe briefly, the standard curves for nitrite were prepared; then the samples (50 µL of serum and 100 µL of tissue suspensions) were added to the Griess reagent. Proteins were precipitated by adding 50 µL of 10% trichloroacetic acid (Sigma-Aldrich). The contents were centrifuged, and the supernatants were transferred to a 96-well flat-bottomed microplate. Absorbance was read at 520 nm using a microplate reader, and the final values were calculated from the standard calibration plots (20).

Statistical analysis

Statistical analysis was performed using SPSS 18. One-way analysis of variance (ANOVA) followed by Tukey's post hoc test was used to conduct data analysis. Values were expressed as mean ± SEM. $P<0.05$ was considered significance level.

Results

Anethole increased seizure threshold

The results showed that anethole at 62.5 and 125 mg/kg as well as diazepam significantly increased the seizure threshold in comparison to the group given normal saline ($P<0.001$; Figure 1).

Anethole decreased nitrite level in the prefrontal cortex

As illustrated in Figure 2, the level of nitrite in the prefrontal cortex in the groups receiving anethole at 31.25 ($P<0.01$), 62.5 ($P<0.001$) and 125 mg/kg ($P<0.001$) significantly decreased when compared to the saline-treated group.

Anethole increased TAC in the prefrontal cortex

As illustrated in Figure 3, the TAC in the prefrontal cortex in the groups treated with anethole at 62.5 ($P<0.001$) and 125 mg/kg ($P<0.001$), as well as diazepam ($P<0.05$) significantly increased in comparison to the saline-treated group.

Anethole decreased the MDA level in the prefrontal cortex

As shown in Figure 4, the MDA level in the prefrontal cortex of the groups receiving anethole at 31.25 ($P<0.01$), 62.5 ($P<0.001$) and 125 mg/kg ($P<0.001$) significantly decreased in comparison to the saline-treated group.

Discussion

Our findings showed that anethole exerted anticonvulsant effect in the PTZ-induced seizure in mice. We observed that anethole decreased nitrite and MDA levels, while it increased the TAC in the prefrontal cortex. The results also demonstrated that anethole probably increased the seizure threshold via its antioxidant properties.

Although standard treatments can control epilepsy attacks, millions of people have uncontrolled epilepsy despite use of chemical anticonvulsants; therefore,

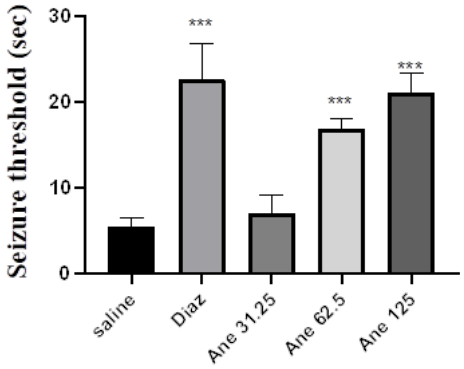

Figure 1. The seizure threshold (in seconds) in experimental groups. Data were presented as mean ± SEM and analyzed using one-way ANOVA followed by Tukey's post-hoc test. ***P<0.001; as compared with the saline-treated group. Diaz: Diazepam; Ane: Anethole.

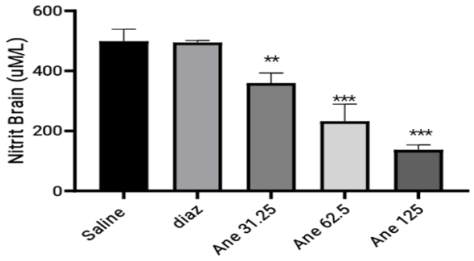

Figure 2. The level of nitrite in the prefrontal cortex in experimental groups. Data were presented as mean ± SEM and analyzed using one-way ANOVA followed by Tukey's post-hoc test. **P<0.001 and ***P<0.001; as compared with the saline-treated group. Diaz: Diazepam; Ane: Anethole.

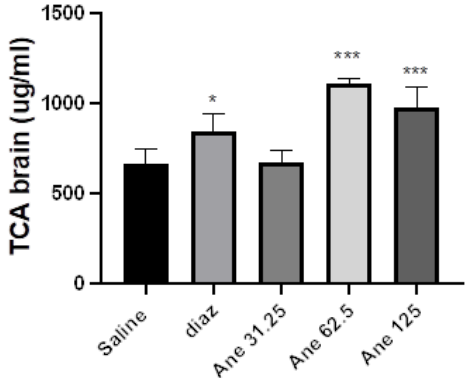

Figure 3. The total antioxidant capacity of the prefrontal cortex in experimental groups; Data were presented as mean ± SEM and analyzed using one-way ANOVA followed by Tukey's post-hoc test, * P<0.05 and *** P<0.001; as compared with the saline-treated group. Diaz: Diazepam; Ane: Anethole.

researches continue to discover new drugs, with higher efficacy and fewer side effects (21). Medicinal plants and their compounds have been used for management of various diseases across the world. Because of their pharmacological effects, effectiveness and low side effects, researchers are considering these compounds as adjuvant therapies for treatment of diseases (22).

Anethole is an alkenyl benzene (1-methoxy-4-(1-propenyl)benzene) present in the essential oils of various plants, mainly fennel, cinnamon, and anise (23). Previous studies have reported several pharmacological properties

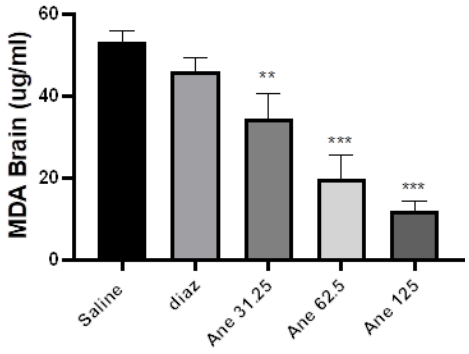

Figure 4. Level of malondialdehyde in the prefrontal cortex in experimental groups. Data were presented as mean ± SEM and analyzed using one-way ANOVA followed by Tukey's post-hoc test, **P <0.01 and *** P <0.001, as compared with the saline-treated group. Diaz: Diazepam; Ane: Anethole.

for anethole, including anti-neuroinflammatory, hepatoprotective, nephroprotective and antidiabetic effects (23-25). Ample evidence has demonstrated neuroprotective effects of the compound. In this regard, previous studies have determined that anethole attenuates behavioral changes following social isolation stress (26), and mitigates neuropathic pain induced by chronic constriction injury (27). In this study, we observed that administration of anethole increased the seizure threshold in PTZ-induced seizure in mice. Our results also showed that anethole could significantly delay the onset of seizure following induction with PTZ.

Previous studies have shown that oxidative stress is involved in the pathophysiology of seizure (28,29). In this regard, it has been shown that agents with antioxidant effects mitigate seizure attacks (30). Researches have shown that increase in the MDA level is associated with proconvulsant effects while decrease in the MDA level is accompanied with anticonvulsant effects (31,32). Furthermore, ample experimental evidence has shown that some agents with potential anticonvulsant effects increase the TAC in the brain and consequently seizure threshold (33,34). In terms of the role of the nitrergic system and NO in the pathophysiology of seizure, it has been determined that there is a direct correlation between NO level and the intensity of seizure (35,36). As well, it has been demonstrated that agents that reduce the levels of nitrite significantly increase the seizure threshold. Furthermore, reducing level of nitrite is involved in the anticonvulsant effects of some anticonvulsants (37,38). In line with aforementioned studies, our results showed that anethole increased TAC and reduced the levels of nitrite and MDA in the prefrontal cortex, indicating that anethole has antioxidant properties and is therefore likely to increase the seizure threshold in the PTZ-induced seizure in mice.

Conclusion

We concluded that anethole, partially at least, exerts anticonvulsant effect (increases seizure threshold) in the PTZ-induced seizure in mice via its antioxidant properties.

Authors' Contribution

SS, SH-D HA-K:performed experiments, wrote the manuscript. JK: analyzed data. MJB: performed experiments. SH-D and HA-K: designed study.

Conflict of Interest Disclosures

The authors declare that there is no conflict of interests.

Ethical Approval

The ethics approval was obtained from Shahrekord University (with the ethical code of IR.SKU.REC.1400.049).

References

1. Amini-Khoei H, Kordjazy N, Haj-Mirzaian A, Amiri S, Haj-Mirzaian A, Shirzadian A, et al. Anticonvulsant effect of minocycline on pentylenetetrazole-induced seizure in mice: involvement of nitric oxide and N-methyl-d-aspartate receptor. Can J Physiol Pharmacol. 2018;96(8):742-50. doi: 10.1139/cjpp-2017-0673.
2. Bazzigaluppi P, Ebrahim Amini A, Weisspapir I, Stefanovic B, Carlen PL. Hungry neurons: metabolic insights on seizure dynamics. Int J Mol Sci. 2017;18(11):2269. doi: 10.3390/ijms18112269.
3. Zhao M, Suh M, Ma H, Perry C, Geneslaw A, Schwartz TH. Focal increases in perfusion and decreases in hemoglobin oxygenation precede seizure onset in spontaneous human epilepsy. Epilepsia. 2007;48(11):2059-67. doi: 10.1111/j.1528-1167.2007.01229.x.
4. Frantseva MV, Perez Velazquez JL, Tsoraklidis G, Mendonca AJ, Adamchik Y, Mills LR, et al. Oxidative stress is involved in seizure-induced neurodegeneration in the kindling model of epilepsy. Neuroscience. 2000;97(3):431-5. doi: 10.1016/s0306-4522(00)00041-5.
5. Shin EJ, Jeong JH, Chung YH, Kim WK, Ko KH, Bach JH, et al. Role of oxidative stress in epileptic seizures. Neurochem Int. 2011;59(2):122-37. doi: 10.1016/j.neuint.2011.03.025.
6. White BC, Sullivan JM, DeGracia DJ, O'Neil BJ, Neumar RW, Grossman LI, et al. Brain ischemia and reperfusion: molecular mechanisms of neuronal injury. J Neurol Sci. 2000;179(S 1-2):1-33. doi: 10.1016/s0022-510x(00)00386-5.
7. Ostadhadi S, Khan MI, Norouzi-Javidan A, Chamanara M, Jazaeri F, Zolfaghari S, et al. Involvement of NMDA receptors and L-arginine/nitric oxide/cyclic guanosine monophosphate pathway in the antidepressant-like effects of topiramate in mice forced swimming test. Brain Res Bull. 2016;122:62-70. doi: 10.1016/j.brainresbull.2016.03.004.
8. Riazi K, Roshanpour M, Rafiei-Tabatabaei N, Homayoun H, Ebrahimi F, Dehpour AR. The proconvulsant effect of sildenafil in mice: role of nitric oxide-cGMP pathway. Br J Pharmacol. 2006;147(8):935-43. doi: 10.1038/sj.bjp.0706680.
9. Bahremand A, Ebrahimi Nasrabady S, Ziai P, Rahimian R, Hedayat T, Payandemehr B, et al. Involvement of nitric oxide-cGMP pathway in the anticonvulsant effects of lithium chloride on PTZ-induced seizure in mice. Epilepsy Res. 2010;89(2-3):295-302. doi: 10.1016/j.eplepsyres.2010.02.001.
10. Modaresi M, Pouriyanzadeh A. Effect of *Ocimum basilicum* hydro alcoholic extract against pentylenetetrazole-induced seizure in mice. Armaghane Danesh. 2013;18(8):615-21. [Persian].
11. Cabral PH, de Morais Campos R, Fonteles MC, Santos CF, Leal Cardoso JH, do Nascimento NR. Effects of the essential oil of *Croton zehntneri* and its major components, anethole and estragole, on the rat corpora cavernosa. Life Sci. 2014;112(1-2):74-81. doi: 10.1016/j.lfs.2014.07.022.
12. Newberne P, Smith RL, Doull J, Goodman JI, Munro IC, Portoghese PS, et al. The FEMA GRAS assessment of trans-anethole used as a flavouring substance. Flavour and Extract Manufacturer's Association. Food Chem Toxicol. 1999;37(7):789-811. doi: 10.1016/s0278-6915(99)00037-x.
13. Coelho-de-Souza AN, Barata EL, Magalhães PJC, Lima CC, Leal-Cardoso JH. Effects of the essential oil of *Croton zehntneri*, and its constituent estragole on intestinal smooth muscle. Phytother Res. 1997;11(4):299-304. doi: 10.1002/(sici)1099-1573(199706)11:4<299::aid-ptr99>3.0.co;2-a.
14. de Siqueira RJ, Magalhães PJ, Leal-Cardoso JH, Duarte GP, Lahlou S. Cardiovascular effects of the essential oil of *Croton zehntneri* leaves and its main constituents, anethole and estragole, in normotensive conscious rats. Life Sci. 2006;78(20):2365-72. doi: 10.1016/j.lfs.2005.09.042.
15. Sá NAR, Bruno JB, Guerreiro DD, Cadenas J, Alves BG, Cibin FWS, et al. Anethole reduces oxidative stress and improves in vitro survival and activation of primordial follicles. Braz J Med Biol Res. 2018;51(8):e7129. doi: 10.1590/1414-431x20187129.
16. Ritter AM, Ames FQ, Otani F, de Oliveira RM, Cuman RK, Bersani-Amado CA. Effects of anethole in nociception experimental models. Evid Based Complement Alternat Med. 2014;2014:345829. doi: 10.1155/2014/345829.
17. Van Erum J, Van Dam D, De Deyn PP. PTZ-induced seizures in mice require a revised Racine scale. Epilepsy Behav. 2019;95:51-5. doi: 10.1016/j.yebeh.2019.02.029.
18. Benzie IF, Devaki M. The ferric reducing/antioxidant power (FRAP) assay for non-enzymatic antioxidant capacity: concepts, procedures, limitations and applications. In: Apak R, Capanoglu E, Shahidi F, eds. Measurement of Antioxidant Activity & Capacity: Recent Trends and Applications. New York: Wiley; 2018. p. 77-106. doi: 10.1002/9781119135388.ch5.
19. Darvishi-Khezri H, Salehifar E, Kosaryan M, Karami H, Alipour A, Shaki F, et al. The impact of silymarin on antioxidant and oxidative status in patients with β-thalassemia major: a crossover, randomized controlled trial. Complement Ther Med. 2017;35:25-32. doi: 10.1016/j.ctim.2017.08.007.
20. Kordjazy N, Haj-Mirzaian A, Amiri S, Ostadhadi S, Kordjazy M, Sharifzadeh M, et al. Elevated level of nitric oxide mediates the anti-depressant effect of rubidium chloride in mice. Eur J Pharmacol. 2015;762:411-8. doi: 10.1016/j.ejphar.2015.06.030.
21. Hitiris N, Brodie MJ. Modern antiepileptic drugs: guidelines and beyond. Curr Opin Neurol. 2006;19(2):175-80. doi: 10.1097/01.wco.0000218235.67840.82.
22. Abdel-Salam OME, Sleem AA, Sayed M, Youness ER, Shaffie N. Capsaicin exerts anti-convulsant and neuroprotective effects in pentylenetetrazole-induced seizures. Neurochem Res. 2020;45(5):1045-61. doi: 10.1007/s11064-020-02979-3.
23. Samadi-Noshahr Z, Ebrahimzadeh-Bideskan A, Hadjzadeh MA, Shafei MN, Salmani H, Hosseinian S, et al. trans-Anethole attenuated renal injury and reduced expressions of angiotensin II receptor (AT1R) and TGF-β in streptozotocin-induced diabetic rats. Biochimie. 2021;185:117-27. doi: 10.1016/j.biochi.2021.03.011.
24. Yan XL, Xu FY, Ji JJ, Song P, Pei YQ, He MJ, et al. Activation of UCP2 by anethole trithione suppresses neuroinflammation after intracerebral hemorrhage. Acta Pharmacol Sin. 2022;43(4):811-28. doi: 10.1038/s41401-021-00698-1.
25. Zhang C, Zhang B, Chen A, Yin Q, Wang H. Trans-anethole attenuates diet-induced nonalcoholic steatohepatitis through suppressing TGF-β-mediated fibrosis. Clin Res Hepatol Gastroenterol. 2022;46(4):101833. doi: 10.1016/j.clinre.2021.101833.
26. Raman S, Asle-Rousta M, Rahnema M. Protective effect of fennel, and its major component trans-anethole against social isolation induced behavioral deficits in rats. Physiol Int. 2020;107(1):30-9. doi: 10.1556/2060.2020.00012.
27. Wang B, Zhang G, Yang M, Liu N, Li YX, Ma H, et al. Neuroprotective effect of anethole against neuropathic pain

induced by chronic constriction injury of the sciatic nerve in mice. Neurochem Res. 2018;43(12):2404-22. doi: 10.1007/s11064-018-2668-7.
28. Lin TK, Chen SD, Lin KJ, Chuang YC. Seizure-induced oxidative stress in status epilepticus: is antioxidant beneficial? Antioxidants (Basel). 2020;9(11):1029. doi: 10.3390/antiox9111029.
29. MacMullin P, Hodgson N, Damar U, Lee HHC, Hameed MQ, Dhamne SC, et al. Increase in seizure susceptibility after repetitive concussion results from oxidative stress, parvalbumin-positive interneuron dysfunction and biphasic increases in glutamate/GABA ratio. Cereb Cortex. 2020;30(12):6108-20. doi: 10.1093/cercor/bhaa157.
30. Loshali A, Joshi BC, Sundriyal A, Uniyal S. Antiepileptic effects of antioxidant potent extract from *Urtica dioica* Linn. root on pentylenetetrazole and maximal electroshock induced seizure models. Heliyon. 2021;7(2):e06195. doi: 10.1016/j.heliyon.2021.e06195.
31. Restuningwiyani S, Ariani A, Sujuti H, Rahayu M, Subandiyah K. Correlation of malondialdehyde (MDA) and C-reactive protein (CRP) level to neurodevelopmental outcome in children after the episode of convulsive type status epilepticus. J Trop Life Sci. 2018;8(3):260573. doi: 10.11594/jtls.08.03.07.
32. Herrera-Calderon O, Santiváñez-Acosta R, Pari-Olarte B, Enciso-Roca E, Campos Montes VM, Luis Arroyo Acevedo J. Anticonvulsant effect of ethanolic extract of *Cyperus articulatus* L. leaves on pentylenetetrazol induced seizure in mice. J Tradit Complement Med. 2018;8(1):95-9. doi: 10.1016/j.jtcme.2017.03.001.
33. Sarahian N, Mohammadi MT, Darabi S, Salem F. The effects of the peroxisome-proliferator activated receptor-alpha agonist, fenofibrate, on the antioxidant capacity of the brain in pentylenetetrazol kindling seizures in mice. React Oxyg Species. 2019;7(19):47-54.
34. Bagheri S, Heydari A, Alinaghipour A, Salami M. Effect of probiotic supplementation on seizure activity and cognitive performance in PTZ-induced chemical kindling. Epilepsy Behav. 2019;95:43-50. doi: 10.1016/j.yebeh.2019.03.038.
35. Faghir-Ghanesefat H, Keshavarz-Bahaghighat H, Rajai N, Mokhtari T, Bahramnejad E, Kazemi Roodsari S, et al. The possible role of nitric oxide pathway in pentylenetetrazole preconditioning against seizure in mice. J Mol Neurosci. 2019;67(3):477-83. doi: 10.1007/s12031-018-1256-2.
36. Rahimi N, Hassanipour M, Yarmohammadi F, Faghir-Ghanesefat H, Pourshadi N, Bahramnejad E, et al. Nitric oxide and glutamate are contributors of anti-seizure activity of rubidium chloride: a comparison with lithium. Neurosci Lett. 2019;708:134349. doi: 10.1016/j.neulet.2019.134349.
37. Haj-Mirzaian A, Ramezanzadeh K, Tafazolimoghadam A, Kazemi K, Nikbakhsh R, Nikbakhsh R, et al. Protective effect of minocycline on LPS-induced mitochondrial dysfunction and decreased seizure threshold through nitric oxide pathway. Eur J Pharmacol. 2019;858:172446. doi: 10.1016/j.ejphar.2019.172446.
38. Amini-Khoei H, Nasiri Boroujeni S, Lorigooini Z, Salehi A, Sadeghian R, Rahimi-Madiseh M. Implication of nitrergic system in the anticonvulsant effects of ferulic acid in pentylenetetrazole-induced seizures in male mice. J Basic Clin Physiol Pharmacol. 2021. doi: 10.1515/jbcpp-2020-0496.

Cite this article as: Salimian S, Habibian-Dehkordi S, Kaboutari J, Amini-Khoei H, Barkhordari MS. Anethole exerted anticonvulsant effect in pentylenetetrazole-model of seizure in male mice: Possible antioxidant effects. Future Nat Prod. 2022;8(1):2–6. doi: 10.34172/fnp.2022.02.