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Red Ginger's Anti-Anxiety Effect on BALB/c Strain Mice (Mus musculus) Pro-Inflammatory and Anti-Inflammatory Measurements as Anxiety Model

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Abstract

There is a correlation between the occurrence of anxiety and the production of inflammatory mediators, and red ginger rhizome is a well-known herbal product with a high content of phenolic and flavonoid compounds that can be used as anti-inflammatories and antioxidants. The aim of study to evaluate the effect of red ginger as antianxiety in mice (Mus musculus) BALB/c strain by measuring levels of TNF-α, IL-6 and IL-10. Anxiety model mice were carried out by giving treatment with the Forced Swimming Test (FST) for 7 days then assessed by carrying out the Elevated Plus Maze for Mice (EPM) test for one day. After the treatment, the anxiety mice model was made, followed by administration of red ginger ethanol extract therapy for 14 days. The distribution of the experimental animal model groups was divided into control groups (KN, K-, K+) and treatment groups (P, P2, P3).There was a significant difference the decreased of the TNF-α levels at the all of treatment groups with red ginger rhizome extract (P1, P2, P3) compared with the control groups (KN, K-) ($p<0.05$), the significantly decreased of IL-6 levels in the three doses treatment group (P1, P2, P3) compared to the control group (K-, K+) ($p <0.05$) and an increase in IL-10 levels in the 50 mg treatment group compared to group K -, statistically not significant ($p>0.05$).In overall, this study suggests that FST stimulation will create anxiety symptoms and behavior as well as impact cytokine levels, namely elevated levels of TNF-α and IL-6. Giving red ginger ethanol extract has the potential to be researched further for reducing anxiety symptoms because it can block pro-inflammatory cytokines by significantly decreased levels of TNF-α, IL-6, and increased IL-10 cytokines a brief abstract about your paper's subject of study.

Keywords: Anxiety model mice, red ginger, FST, EPM, TNF-α, IL-6, IL-10.

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Introduction

Anxiety is the most commonly reported psychiatric condition, causing a wide range of psychological effects on mental health crises, including factors related to work, finance, micro and macroeconomics, crime, bullying, and social isolation pressures, all of which are thought to be factors in the rise of anxiety disorders[1]. Anxiety is defined by awareness, such as nervousness and fear, and physiological sensations, such as sweating and palpitations, which generate feelings of discomfort and unjustified fear and are generally accompanied by autonomic symptoms[2]. Anxiety feelings are comparable to those of fear, but anxiety differs in that it responds to unreal danger and predicts approaching danger that may or may not occur[3].

The high prevalence of anxiety disorders and the need for anxiety treatment continue to cause many side effects, particularly cardiovascular, gastrointestinal, and hepatotoxic, resulting in complications such as seizures, suicide, sexual dysfunction, weight gain, hypo sodium, insomnia, and hypersomnia, even in patients with cardiovascular problems and diseases of the brain nerves[4].

The Increased inflammatory activity is regarded to be a crucial mediator in the development of anxiety and therefore it was necessary to measure the levels of pro-inflammatory cytokines, such as Tumor Necrotic Factor-α (TNF-α), interleukin-6 (IL-6), anti-inflammatory interleukin-10 (IL-10), and inflammatory markers systemic C-Reactive Protein (C-RP)[5].

Pharmacological interventions with drugs such as using Selective Serotonin Reuptake Inhibitors (SSRIs) are the first line of treatment for anxiety disorders, various classes of antidepressant drugs include Selective Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Tricyclic Anti-Depressants (TCAs) and Monoamine Oxidase Inhibitors (MAOIs), anxiolytics such as benzodiazepines, non-benzodiazepine hypnotics, also used in the treatment of anxiety disorders and depression, However, the use of medicinal compounds in the treatment of various disease causes many side effects and costs quite a lot of money if these drugs are used long term[6,7], so an alternative to the use of herbs is sought, which is quite easy to obtain and inexpensive, regular use or regular consumption does not cause significant side effects, so the selection of herbal ingredients can be considered for safety as a therapeutic treatment[8].

Red ginger is a variant of the species *Zingiber officinale* that is cultivated in Indonesia and Malaysia. Because red ginger has many benefits, particularly as an anti-inflammatory, antimicrobial, antioxidant, antiulcer, anti-clotting, anticancer, and immunostimulant[9]. The aim of the study is to determine the effect of red ginger ethanol as antianxiety in male mice induced into anxiety with Force Swimming Test (FST) and Elevated Plus Maze for Mice (EPM) as evaluation by measuring the duration and measuring the number of open and closed mice arms that entered in anxiety model mice, then measuring molecular proteins such as TNF-α, IL-6 as inflammatory mediators and IL-10 as an anti-inflammatory mediator.

Materials and Methods

Red ginger rhizome *(Zingiber officinale* Rosc. *Var. Rubrum)*

The red ginger used is fresh whole red ginger rhizome (*Zingiber officinale* Rosc. Var. Rubrum) purchased at the Lau Chi traditional wholesale market in Simpang Selayang Village, Medan Tuntungan District, and North Sumatra Province. Using E-Science Services BRIN, identify plants at the Bogor Cibinong Scientific Collections Management Laboratory Research Facilities and Science Technology area in Jakarta. Alkaloids, flavonoids, glycosides, saponins, tannins, and steroids/terpenoid were found in the red ginger rhizome's phytopharmacological screening results by spectrophotometer method.

Research Sample

Anxiety in BALB/c white mice (Mus musculus) aged 2.5-3 months and weighing 18-30 grams. Estimation of sample size using Federer's formula

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(Federer 1965, in Hanafiah 2010) for studies with an experimental design. From the calculation results, the minimum sample size is 24 mice divided into 6 groups. To anticipate the possibility of mice dropping out, group were added, so that the total number of mice used was 30 mice (5 mice per group). The inclusion criteria were, male, 2.5-3 month old, weighing between 18-30 grams, healthy and active in appearance (eating and drinking, no injuries, body defects or hair loss) during the study. The exclusion criteria were mice that suffered other diseases or injuries during the study and mice that did not survive to the end of the study.

Anxiety Model Mice

Male BALB/c mice (8 weeks old, 18-30 gram) were used in this study. They were kept in the animal house under appropriate conditions with free access to food and water. They underwent different stressors to exhibit anxiety-like behaviors in different periods Six groups of animals (normal control, negative control (treated and intervened with suspension agent Carboxy Methyl Cellulose Sodium (CMC-Na) 0.5%), positive control group (K+) were given Sertraline 50 mg treatment and intervention which was converted to mice weighing 20 grams as much as 0.13 mg and if the weight was 30 grams converted to 0.195 mg. All the treatment groups were given the Forced Swimming Test (FST) and EPM evaluation, and then were treatment with the red ginger ethanol extract dose 50 mg/kg BW (P1), dose of 100 mg/kg BW (P2) and dose of 200 mg/kg BW (P3).

Anxiety model mice were treated with the Forced Swimming Test (FST) and assessed with the Elevated Plus Maze for Mice (EPM). The purpose of this EPM test is to count the number of open and closed arms in mice that enter the labyrinth, as well as the time it takes for the arms to open and close. This FST treatment lasted 7 days and was followed by Elevated Plus Maze for Mice (EPM) for one day. After generating anxiety mouse models, therapy with red ginger ethanol extract was given for 14 days.

Examination of Molecular Protein

All mice were sampled by withdrawing blood from an orbital vein (4ml/ mouse), blood was collected in serum separator tubes (SST), and samples allowed to clot overnight at 4 degrees Celsius before centrifugation for 15 minutes at 1000×g. The serum was removed for assay immediately.

The measurement of molecular protein such as TNF-α, CRP, IL6 and IL 10 with ELISA methods in laboratory of the Institute of Biosciences, University of Brawijaya Malang.

Statistical Analysis:

The statistical analysis was carried out using SPSS version 20.0 using *analysis of variance (ANOVA) test* and to be continued by post hoc LSD analysis and *Kruskal-Wallis* and to be continued by *Mann Whitney* analysis. P-values less than 0.05 ($p < 0.05$) were considered statistically significant[10].

Results and discussion

Results

The results of the extract's phytochemical screening found the presence of flavonoids, phenolic, saponins, alkaloids and steroids/terpenoids and no tannins were found and for determining of the levels of secondary metabolites from the ethanol extract of red ginger obtained flavonoid levels of 43.97 mg QE/g extract, phenol levels of 97.22 mg GAE/g extract and anti-oxidant levels (IC50) of 38.86 ppm.

In this study, involves various groups: a normal control group (KN) with no treatment, a negative control group (K-) treated with 0.5% CMC-Na suspending agent, a positive control group (K+) treated with sertraline 50 mg, converted to 0.13 mg for 20-gram mice and 0.195 mg for 30-gram mice. Additionally, there are three treatment groups: P1 receiving a 50 mg dose of red ginger ethanol extract (Zingiber officinale Rosc. Var. Rubrum), P2 with a 100 mg dose, and P3 with a 200 mg dose.

The group of mice given the *Forced Swimming Test* (FST) treatment showed anxiety, as showed by a reduced number of open arms in the FST group and also when compared to the control group, but there was no statistically significant difference $p>0.05$, but in the FST treatment with an assessment of the number of closed arms a significant difference was found in the control group and the treatment group, $p<0.05$, and with the post hoc *One Way ANOVA test*

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analysis found significant differences in the number of closed arms in the normal control group (KN) with the (K-) group, the (K+) group, and the treatment group (P1, P3), in the (K+) group there was a difference significantly the number of closed arms in the P2 group, P1 group there is a significant difference in the number of closed arms with the P2 group and P2 group there is a significant difference in the number of open arms in the P3 group, p<0.05.

Table 1. EPM Assessment of FST treatment in the mice group (Number of open and closed arms)

Groups	Median (min-max) The count of opened arms	p value	Median (min-max) The count of closed arms	p value	Post hoc				
					K-	K+	P1	P2	P3
KN	4 (3-5)		2 (1-3)		0.00**	0.00**	0.00**	0.181	0.00**
K-	2 (1-4)		5 (3-7)			0.785	1.000	0.006	0.181
K+	3 (1-5)	0.068*	6 (3-7)	0.00**			0.785	0.003**	0.281
P1	3 (2-5)		5 (4-7)					0.006**	0.181
P2	2 (1-2)		3 (2-4)						0.00**
P3	3 (2-5)		6 (5-7)						

Note: Data is in median form
*p <0.05 statistically significant, *Kruskal-Wallis test*
KN = normal group K-= CMC group K + = sertraline group
P1=extract dose 50 mg group P2=extract dose 100 mg group P3=extract dose 200 mg group
**p<0.05, *One Way ANOVA test*

Through the Elevated Plus Maze for Mice (EPM) test with an assessment of the duration of time required for open arms in mice, there was a significant difference in the treatment group compared to the control group, p <0.05., with the Man Whitney post hoc test, found a significant difference duration of open arms in the KN group with the K-, K+ and treatment groups P2, P3 p<0.05. We can see on the table 2.

Table 2. EPM assessment of the FST treatment in the mice group (Duration time of open arms)

Groups	Median (min –max) Duration of opened arms te (sec)	p value	Post Hoc				
			K-	K+	P1	P2	P3
KN	52 (42-80)		0.008**	0.008**	0.056	0.008**	0.008**
K-	20 (9- 34)			0.548	1.00	0.222	0.690
K+	25 (11-31)	0.023*			1.00	0.222	0.310
P1	13 (9-54)					0.310	1.00
P2	10 (7-34)						0.548
P3	20 (6-26)						

Note: Data is in median form
*p <0.05 statistically significant, *Kruskal-Wallis test*
KN = normal group K-= CMC group K + = sertraline group
P1=extract dose 50 mg group P2=extract dose 100 mg group P3=extract dose 200 mg group.
**p<0.05, *Mann Whitney test.*

While the (EPM) test on the assessment of the duration of time required for closed arms in mice was significantly different in the treatment group compared to the control group, p <0.05., with the Man Whitney post hoc test, found a significant difference duration of open arms in the KN group

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with the K-, K+ and P2 treatment groups, p<0.05. We can see on the table 3.

Table 3. EPM assessment of the FST treatment in the mice group (Duration time closed arms)

Groups	Median Duration of closed arms (sec)	p value	K-	K+	P1	P2	P3
KN	248 (220-258)		0.008**	0.008**	0.056	0.008**	0.095
K-	280 (266-291)			0.548	1.000	0.222	1.00
K+	275 (269-289)	0.045*			1.000	0.222	0.841
P1	287 (246-291)					0.310	0.841
P2	290 (266-293)						0.421
P3	278 (220-294)						

Note: Data is in median form
*p <0.05 statistically significant, *Kruskal-Wallis test*
KN = normal group K-= CMC group K + = sertraline group
P1=extract dose 50 mg group P2=extract dose 100 mg group P3=extract dose 200 mg group. **p<0.05, *Mann Whitney* test

The Effect of TNF-α Levels on Anxiety Model Mice Treated

The examination of TNF-α levels in the serum, there was a significant difference in average TNF-α levels between the two groups, namely the control and treatment groups (with a significance level of p<0.05). Furthermore, the results showed that TNF-α levels tended to significantly decrease in the treatment group at three different dose levels (P1, P2, P3) when compared to the control group (referred to as KN and K- in the study).

In addition, through the post hoc analysis test, it can also be observed that there is a significant difference in the mean TNF-α levels between the untreated control group (K-) and the treated control group (K+), as well as between the treated groups at all doses (P1, P2, P3) and the untreated control group (K-) as shown in table 4.

Table 4. TNF-α levels in normal mice and anxiety model

Groups	TNF-α serum (pg/ml) mean±SD	p value	Post Hoc				
			K-	K+	P1	P2	P3
KN	4.24±0.9[6]		0.327	0.815	0.755	0.997	0.690
K-	5.28±2.140			0.020**	0.015**	0.135	0.011**
K+	3.613±0.556	0.007*			1.00	0.972	1.00
P1	3.56±0.863					0.95	1.00
P2	4.00±0.926						0.92
P3	3.50±0.515						

Note: Data is in the form of mean ± SD
*p <0.05 statistically significant, *one-way ANOVA test*
KN = normal group K-= CMC group K + = sertraline group
P1=extract dose 50 mg group P2=extract dose 100 mg group P3=extract dose 200 mg group
**p<0.05, post hoc test.

The Effect of IL-6 Levels on Anxiety Model Mice Treated

The measurement of IL-6 levels in the control and treatment groups of mice, found IL-6 levels in the KN group 23,168 (23,159-23,179) pg/ml, K- group 23,199 (23,171-23,547) pg/ml, K+ group 23,186 (23,178-23,202) pg /ml, treatment group P1 23.185 (23.181-23.225) pg/ml, P2 23.172 (23.161-23.228) pg/ml, P3 23.177 (23.168-23.179) pg/ml, there was a significant difference in. A decrease in IL-6 levels was found in the treatment group at the three doses (50,100,200) mg compared to the control group (K-, K+). With *post hoc test* analysis found a significant difference in mean IL-6 levels in the normal group

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(KN) with the K- and K+ groups, the K+ group with the 50 dose treatment (P1) as shown in the table 5.

Table 5. IL-6 levels in the anxiety model mice

Groups	IL6 (Pg/ml)	p value	Post Hoc				
	Median (min-max)		K-	K+	P1	P2	P3
KN	23.168 (23.159-23.179)		0.056**	0.016**	0.008	0.421	0.31
K-	23.199 (23.171-23.547)			0.841	1.00	0.421	0.222
K+	23.186 (23.178-23.202)	0.041*			0.690	0.548	0.016**
P1	23.185 (23.181-23.225)					0.548	0.008**
P2	23.172 (23.161-23.228)						1.00
P3	23.177 (23.168-23.179)						

Note: Data is in the form of median (min-max)
*p <0.05 statistically significant, *Kruskall-Wallis Test*
KN = normal group K-= CMC group K + = sertraline group
P1=extract dose 50 mg group P2=extract dose 100 mg group P3=extract dose 200 mg group
**p<0.05, *Mann Whitney test*

Effect of IL-10 Levels in Anxiety Model Mice

IL-10 levels showed a increased in the group of treated anxiety mice (P1) compared to the group of the control group (K-), but statistically there was no significant difference as shown in table below table 6.

Table 6. IL-10 levels in the anxiety group of mice

Groups	IL10 serum (pg/ml) Mean±SD	p value
KN	469.719±.0.0381	
K-	469.671±0.0372	
K+	469.703±0.0205	0.56
P1	469.706±0.0074	
P2	469.689±0.0745	
P3	469.690±0.0415	

Note: Data is in the form of mean ±SD
*p <0.05 statistically significant, One *Way ANOVA test*
KN = normal group K-= CMC group K + = sertraline group
P1=extract dose 50 mg group P2=extract dose 100 mg group P3=extract dose 200 mg group

Discussion

The results of the extract's phytochemical screening found the presence of flavonoids, phenolic, saponins, alkaloids and steroids/triterpenoids and no tannins were found. The test results for determining the levels of secondary metabolites from the ethanol extract of red ginger obtained a flavonoid level of 43.97 mg QE/g extract, phenol content. 97.22 mg GAE/g extract and Anti-oxidant level (IC50) 38.86 ppm.

Natural antioxidants derived from red ginger rhizome are linked to phenolic, flavonoid, and carotenoid content. Previous research revealed that the phenolic content detected in red ginger rhizome was (931.94 mg GAE/100 g) and that it was significantly associated with as an antioxidant in this study[11].

It was carried out in the anxiety model mice study by administering the *Force Swimming Test* treatment and assessing it with EPM. In this study, each mouse was placed in a container with a diameter of 20 cm and a height of 30 cm filled with water at a temperature of 250 C and a water level of 15 cm and allowed to swim for 6 minutes before being removed and allowed to dry for one hour.

This is evidenced by the significantly decreased number of open arms in the FST group when compared to the control group. The *Force Swimming Test*, sometimes known as the Porsolt Swim Test, has sparked debate. The FST was

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developed in the 1970s by Roger Porsolt as a rapid detection of behavior for antidepressant drugs and it is currently regarded the gold standard of animal testing for depression[12].

The period of time required for the Elevated Plus Maze *test* was considerably shorter and the number of open arms was lower in the FST treatment group compared to the control group. According to the habit of avoiding open arms is thought to be the outcome of increased anxiety. This EPM test has high predictive validity when used to screen for anxiolytic medications[13].

In the study, we found that there was a significant difference in the duration of the opened and closed arms in the control group and the treatment group ($p < 0.05$), We found that there was the shorter duration of the opened arms in the treatment group with a dose of 50 and 100 mg ($p<0.005$) compared to the three control groups, while the duration of closed arms was found to be longer in the three treatment groups (P1, P2, P3), but the longest duration was the treatment group with a dose of 100 mg.

There was no statistically significant difference ($P>0.05$) between the treatment group with a dose of 100 and the KN and K- groups although the fact that there were less open arms in the treatment group. The treatment group with a dose of 100 was found to have less closed arms than the control group K-, the K+ group, but more closed arms than the KN group, and this difference was statistically significant. The present study is consistent with the research[14].

Other studies state that the EPM test has weaknesses such as variables that cannot be controlled, such as existing procedural differences, and that it is difficult to replicate for more specific results. The Porsolt forced swimming test, anxiety in a bright room, light/dark and open room transition tests, and open field testing are other procedures that can be utilized for anxiety conditioning[15].

Several studies have found that depression and anxiety are associated with increased peripheral inflammatory markers such as C-RP, IL-6, and TNF-α, as well as blood cytokines[16]. Previous research has revealed that inflammation affects brain areas associated with anxiety, particularly the *amygdala, insula, and anterior cingulate cortex*, which appears to be caused by cytokine effects on monoamines and glutamate[17]. Other research stated that CRP that as biomarker that severe cases in infection of COVID-19[18].

Psychological stress affects the immune system in many ways. The effect of stress on the immune system varies and can be individual specific[19]. The most frequently observed response is immune suppression, especially when stress is chronic and persistent. Several studies have suggested that there is a relationship between TNF-α secretion and anxiety[20]. In this study there was a significant difference in TNF-α levels in the control group and the treatment group ($p<0.05$). In the use of ethanol extract of red ginger rhizome, there was a significant decrease in TNF-α levels at doses of 50 mg and 200 mg ($p<0.05$). Previous research stated that potential therapeutic strategies for mood disorders are compounds that can reduce TNF-α or compounds that are selectively anti-TNF-α[21].

Studies show that of the many cytokines, IL-6 is one of the most studied cytokines in terms of its relation to depression[22]. Evidence has been carried out from various studies either through experimental animals or clinically showing that there is an increase in peripheral and central cytokines and IL-6 plays an important role in stress reactions and depressive disorders, and increased release of IL-6 is a factor associated with the prognosis of Major Depression Disorder and It is also a therapeutic response, and may contribute to various depressive symptoms[23]. In this study, a decrease in IL-6 levels was found in the treatment group at doses of 100 and 200 mg compared to the control group, so the red ginger extract used can reduce anxiety with evidence of decreased IL-6 in the treatment group and statistically found a significant decreased with the control group ($p<0.05$).

Pro-inflammatory and anti-inflammatory cytokines are in a balanced state in healthy people, with IL-6 mediating the early stages of inflammation and then triggering the release of IL-10, which has immunoregulatory effects and suppresses inflammation, that pro-inflammatory cytokines play an important role in intercellular communications[24].

In individuals in good health, there is a regulated balance of pro- and anti-inflammatory cytokines, such as IL-6, which mediates the initial phase of the inflammatory process and then causes the

production of IL-10, which has immunoregulatory effects and overcomes inflammation[25]. These findings clearly show that the immune system can respond immediately to inflammation and then return to a homeostatic state. The immunoregulatory balance between pro- and anti-inflammatory cytokines is a crucial mechanism in anxiety-related inflammatory diseases. In this case, it might be argued that depressed patients have lower levels of IL-10 and higher levels of pro-inflammatory cytokines. The decreased of IL-10 levels will prevent inflammation repair, impair pro-inflammatory inhibition in undamaged tissue, and allow the adverse development of acute to chronic inflammation[26].

Giving red ginger in this study showed that there is a repair mechanism that responds to inflammation to maintain homeostasis. This was proved by an increase in IL-10 levels in the group that received therapy at both doses of 50 mg/kg, 100 mg/kg BW, and 200 mg/kg BW against pro-inflammatory cytokines such as TNF-α and IL-6, as it is well known that treatment increases IL-10 levels[27].

Conclusion

In general, this study indicates that FST stimulation will cause anxiety and cause anxiety symptoms and behavior and affect cytokine levels, namely increased levels of TNF-α and IL-6. Giving red ginger can inhibit pro-inflammatory cytokines by markedly decreasing levels of TNF-α, IL-6 and increasing IL-10 cytokines and has the potential to be studied further to reduce anxiety symptoms.

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Author's Declaration

- Conflicts of Interest: None.
- We hereby confirm that all the Tables in the manuscript are ours.
- The author has signed an animal welfare statement.
- Ethical Clearance: The project was approved by the local ethical committee at the Faculty of Medicine, Universitas Sumatera Utara, Indonesia (approval No.547 /KEPK/USU/2022).

Authors' Contributions

I.A.D as corresponding author, designed the study perform by I.A.D, A.S.R, U.H, E.E, performed the experiments study I.A.D, A.S.R, U,H, E.E, Analyzed the data by I.A.D, E.E, T.W, Wrote the paper with input from all authors by S.I, M.M.A and M.R.

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تأثير الزنجبيل الأحمر المضاد للقلق في BALB / c الفئران (Musculus) قياسات مسببة للالتهابات ومضادة للالتهابات كنموذج لدراسة القلق

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الخلاصة

هناك علاقة بين حدوث القلق وإنتاج الوسائط الالتهابية ، جذور الزنجبيل الأحمر هو منتج عشبي مشهور يحتوي على نسبة عالية من مركبات الفينول والفلافونويد التي يمكن استخدامها كمضادات للالتهابات ومضادات الأكسدة. دراسة لتقييم تأثير الزنجبيل الأحمر كمضاد للقلق لدى الفئران (Mus musculus) سلالة BALB / c عن طريق قياس مستويات TNF-α و IL-6 و. IL-10.

تم إجراء اختبار نموذج القلق من خلال إعطاء العلاج للفئران باختبار السباحة القسرية (FST) لمدة 7 أيام ثم تم تقييمها عن طريق إجراء اختبار Elevated Plus Maze for Mice (EPM) لمدة يوم واحد. بعد العلاج ، تم عمل نموذج الفئران القلق ، متبوعًا بإعطاء العلاج بمستخلص الإيثانول من الزنجبيل الأحمر لمدة 14 يومًا. تم تقسيم توزيع مجموعات النماذج الحيوانية التجريبية إلى مجموعات ضابطة (KN، K-، K +) ومجموعات معاملة (P، P2، P3) وكان هناك اختلاف معنوي في انخفاض مستويات TNF-α في كل المعاملة. المجموعات التي تحتوي على مستخلص جذور الزنجبيل الأحمر (P1، P2، P3) مقارنة بمجموعات التحكم (KN ، (P <0.05) (K- ، انخفض بشكل ملحوظ م من مستويات IL-6 في مجموعة العلاج بالجرعات الثلاث (P1، P2، P3) مقارنة بالمجموعة الضابطة (K-)، (p <0.05) (+ K وزيادة مستويات IL-10 في مجموعة العلاج 50 مجم مقارنة بالمجموعة K - ، غير ذات دلالة إحصائية (p> 0.05). تشير الدراسة إلى أن تحفيز FST سيخلق أعراضًا وسلوكًا للقلق بالإضافة إلى تأثيره على مستويات السيتوكين ، أي المستويات المرتفعة من TNF- و IL-6. إن إعطاء مستخلص الإيثانول من الزنجبيل الأحمر لديه القدرة على إجراء مزيد من البحث لتقليل أعراض القلق لأنه يمكن أن يمنع السيتوكينات المؤيدة للالتهابات عن طريق انخفاض مستويات TNF- و IL-6 وزيادة السيتوكينات IL-10 بشكل كبير. يذاكر.

الكلمات المفتاحية: الفئران نموذج القلق ، الزنجبيل الأحمر، FST، MPE، TNF-α، IL-6، IL-10.