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Ginger honey affects cortisol, estrogen and glutathione levels; preliminary study to target preconceptional women☆

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ABSTRACT

Objective: This study was aimed to determine the effect of ginger honey supplementation on cortisol, glutathione, and estrogen levels. The study was conducted on mice that had not yet experienced conception, and prior stress induction was carried out so that they could be continued for human trials at the preconception stage and subjects who experienced mild stress.
Method: It was an in vivo study, pretest–posttest control group design. The sample of this study was 2–3 months female Balb/c mice, divided into negative control and ginger honey intervention as much as 28 mg/20 g BW for 14 days—the ELISA method used to examine cortisol hormone, glutathione levels, and estrogen levels. The mice chosen were those that had never experienced conception, and before the intervention, swimming activities were carried out on the mice until they showed symptoms of stress.
Results: Results show 42 mg/20 g BW of ginger honey administration for 14 days increased 1.892 ng/dl of cortisol (p = 0.165), increased 2.438 ng/dl of glutathione (p = 0.002), and also increased 22.754 ng/ml estrogen levels in induced stress Balb/c female mice (p = 0.001).
Conclusion: Ginger honey did not affect reducing cortisol levels but increasing glutathione and estrogen levels significantly. Ginger honey supplements are the potential to use as complementary therapies.

Introduction

The significant ways to improve the quality of the preconception phase are to improve nutritional status.[1] Nutrition is associated with increasing the cortisol hormone as a physiological response to stress that is secreted by the adrenal cortex.[2–4] Working women, during menstruation, pregnancy, childbirth, postpartum, and menopause, are more likely to experience stress up to two times more than men.[2,5,6]

Glutathione hormone is related to oxidative stress. It is a state of imbalance between reactive oxygen species (ROS) and the ability of biological systems to reduce ROS levels.[7] These conditions can cause several reproductive diseases such as endometriosis, PCOS, decreased oocyte quality, infertility, miscarriage, preeclampsia, IUGR, and premature birth [8,9] occurrence of Polycystic Ovarian Syndrome (PCOS) associated with reproductive and metabolic diseases, and this condition is characterized by irregular menstruation, oligomenorrhea or amenorrhea, anovulation.[10]

The state of oxidative stress at the cellular level can affect the quality of the women's and men's reproductive organs, decrease fertility, and increase the risk of abortion, and fetal growth is inhibited due to excessive exposure to glucocorticoid hormones.[11] Oxidative stress has been linked to many patterns of disease.[12] The body's main antioxidant, glutathione, has an important role in preventing cell damage caused by oxidative stress [13] and is able to maintain vitamin C and vitamin E, which also acts as exogenous antioxidants.[14]

Low levels of estrogen and stressful conditions also trigger women to be vulnerable to oxidative stress. Previous studies in experimental animals have suggested that high corticosterone levels are associated with low estradiol and have a negative effect on mood,[15] low estrogen levels leading to amenorrhea and irregular menstruation.[16] Young women and menopausal women who experience decreased estrogen are more at risk for autoimmune disease.[17]

The provision of ginger containing antioxidants can reduce oxidation activity,[18] and the ethanol content of ginger increases enzymatic antioxidant activity.[19] Ginger can also replace the role of mefenamic acid (NSAIDs) in reducing menstrual pain in women.[20]

Honey with antioxidant content such as flavonoids, phenolic acids, enzymes, vitamins (A, E, C),[21] and a minor mineral (copper and iron)[22] can prevent cancer, heart disease, infectious diseases, decreased neurological function, inflammation, and aging.[21] Honey administration to 2 months mice affects brain development and

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memory and reduces these mice's anxiety level.[23] Administration of Tualang honey in induced stress mice can reduce ACTH and corticosterone levels, reduce MDA, and increase antioxidant activity in the brain.[20]

It takes innovations to helps humans reduce stress in the preconception phase to effort a healthy reproduction. Therefore, we need an intervention with minimal side effects on the body; one of the alternatives is those derived from natural ingredients or food. Honey and ginger are two natural ingredients whose acceptance for consumption is very easy for people. This study is expected to contribute as primary research for preconception problems, especially in subjects with mild stress. It is also expected to strengthen the use of inexpensive natural ingredients to solve health problems and impact local honey entrepreneurs by increasing sales.

This study strengthens previous research conducted by the team because it needs to check the reliability of the previous study, except that the previous study used two doses and examined each hormone separately. The study was repeated using the highest dose and evaluating the hormone simultaneously.[24–27]

Methods

This research was an in vivo laboratory research and is carried out in the Biopharmacy Laboratory and the Microbiology Laboratory of the Teaching Hospital of Hasanuddin University with a pretest–posttest control group research design. Honey and ginger were local products from south Sulawesi, Indonesia.

The sample of this study was female Balb/c mice aged 2–3 months, divided into 2 groups (5 of each group). Group 1 as a control group) is given standard feed, and group 2 as ginger honey as much as 42 mg/20 g BW is given by oral sonde and standard feed for 14 days. Before administering the intervention, the mice were given swimming treatment for 15 min to increase the stress state. The examination of cortisol hormone levels, glutathione levels, and estrogen hormone levels is carried out using the ELISA method on the 15th day. 2. This research was approved by The Ethics Committee of Faculty of Medicine, Hasanuddin University.

Result

The analysis results showed that ginger honey increased 1.892 ng/ml of the hormone cortisol, although this increase was not significant ($p = 0.165$). However, this increase was still lower than the control group, which increased its cortisol hormone to 3.450 ng/ml, although it was also not significant ($p = 0.064$) (Table 1).

Table 2 shows that ginger honey significantly increased glutathione hormone levels by 2.438 ng/ml ($p = 0.002$), while the control group showed a decrease in glutathione levels by 0.148 ng/ml ($p = 0.554$).

Table 3 shows a significant increase in estrogen levels of 22.754 ng/ml ($p = 0.001$) compared to the control group, which increased by 3.598 ng/ml ($p = 0.134$).

Table 1
Analysis of cortisol hormone levels.

Time	Cortisol level (ng/ml)	
	Control	*Ginger Honey* Mean ± SD
Pre	8.029 ± 0.579	8.041 ± 0.218
Post	11.480 ± 3.331	9.933 ± 2.367
Different Mean	+3.450	+1.892
*p-value	0.064	0.165

* Paired *T*-test.
Description: Ginger Honey: Cortisol level.

Table 2
Analysis of glutathione hormone level.

Time	Glutathione hormone level (ng/ml)	
	Control Mean ± SD	*Ginger Honey* Mean ± SD
Pre	0.986 ± 0.781	0.588 ± 0.158
Post	0.837 ± 0.744	3.026 ± 0.810
Different Mean	−0.148	2.438
*p value	0.554	0.002

* Paired *T*-test.
Description: Ginger Honey; glutathione.

Table 3
Analysis of estrogen hormone level.

Time	Estrogen hormone level (ng/ml)	
	Control Mean ± SD	*Ginger Honey* Mean ± SD
Pre	2.253 ± 1.029	3.476 ± 3.461
Post	5.851 ± 4.506	26.230 ± 3.839
Different Mean	3.598	22.754
*p value	0.134	0.001

* Paired *T*-test.
Description: Ginger Honey; glutathione.

Based on the data of Table 4, in the Intervention group, ginger honey had the most significant effect on increasing estrogen level hormone by 22.754 ng/ml ($p = 0.001$).

Discussion

As much as 42 mg/20 g BW in female Balb/c mice, Ginger honey can increase glutathione and estrogen levels that handle oxidative stress and increase cortisol levels insignificantly.

Glutathione exists in almost all body cells that act as antioxidants, hydrogen donors, to free radicals to prevent oxidative stress.[29,30] Oxidative stress is a trigger for PCO disease, oocyte damage, and infertility.[31] A mixture of ginger and gelam honey can overcome oxidative stress conditions in diabetes mellitus patients by decreasing ROS production by increasing Glutathione levels in the blood.[32] Our research shows that the administration of ginger honey supplements can significantly increase glutathione levels by 0.447 ng/ml. In a previous study on 12 Sprague Dawley rats given Gelam honey as much as 2.5 ml/kg BW, which is equivalent to 1 tsp

Table 4
Differences in cortisol hormone levels, glutathione estrogen hormone levels before and after intervention in balb/c female mice in the ginger honey group.

Time	*Ginger Honey*		
	Cortisol Hormone (ng/dL)	Glutathione Hormone (ng/dL)	Estrogen Hormone (ng/dL)
Pre-test	8.041 ± 0.218	0.588 ± 0.158	3.476 ± 3.461
Post-test	9.933 ± 2.367	3.026 ± 0.810	26.230 ± 3.839
Diff. Mean	+1.892	2.438	22.754
*p value	0.165	0.002	0.001

* Paired *T*-test.
Description: Ginger honey; cortisol: glutathione; estrogen.

for adults in 8 months, can reduce levels of MDA and levels of DNA damage.[33] Previous research also states that Rambutan Honey contains flavonoids and phenolic as a natural antioxidant which plays a role in reducing lipid peroxide and free radicals.[9]

The existence of stressful conditions can suppress the circulation of gonadotropins and steroid hormones, which will result in the disruption of the menstrual cycle. The decrease in GnRH is due to the increased secretion of CRH.[16] On the other hand, an increase in LH, testosterone due to metabolic disorders in the body can cause infertility due to ovulation abnormalities. The provision of ginger in mice with ovulation abnormalities can improve and be effective in balancing the hormones LH, FSH, estrogen, and progesterone.[28]

Conclusion

Ginger honey affects reducing cortisol levels, increasing glutathione and estrogen levels. Therefore, ginger honey supplements are the potential to use as complementary therapies. The limitation of this study is that it only tested one dose and did not compare it with positive controls given anti-depressants. Future studies can test this product on humans with preconception subjects who experience mild stress.

Conflict of interest

The authors declare no conflict of interest.

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