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Curriculum Vitae

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3. Alamat : Jl. Dayak Tunjung Blok F No. 13
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B. Riwayat Pendidikan

1. Pendidikan Formal:
   a. Tamat SD 2007 di SD Muhammadiyah 1 Samarinda
   b. Tamat SMP tahun 2010 di SMP Negeri 9 Samarinda
   c. Tamat SLTA tahun 2013 di SMA Negeri 2 Samarinda
   d. Tamat Perguruan Tinggi Jurusan Sarjana Terapan Kebidanan tahun 2017 di Politeknik Kesehatan Kementerian Kesehatan Kalimantan Timur
2. Pendidikan Non Formal:
   a. Pelatihan BTCLS tahun 2017
   b. Pelatihan PPGDON tahun 2017

C. Pekerjaan dan Riwayat Pekerjaan

Pegawai di Klinik Bersalin dan Umum sebagai Bidan Pelaksana

Lampiran

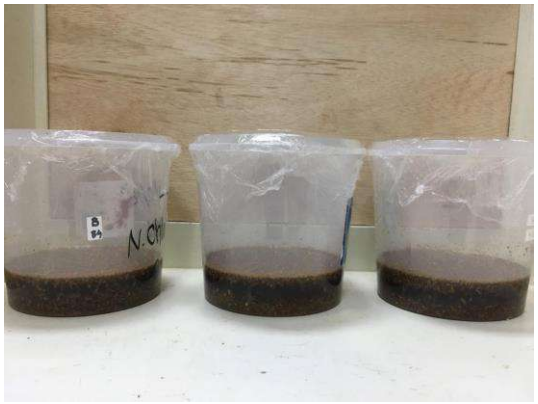
Dokumentasi

Proses Pembuatan *Ginger Honey*

Gambar 1. Pencucian Jahe

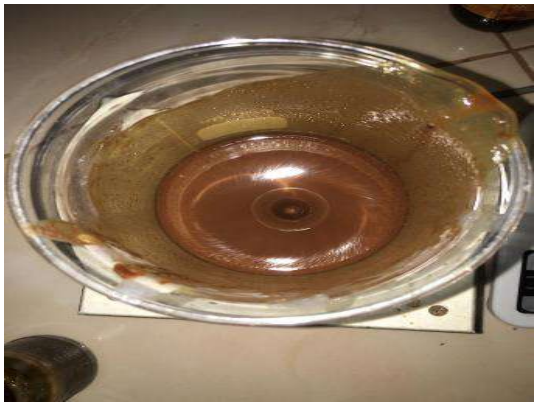
Gambar 2. Pengirisan Jahe

Gambar 3. Pengeringan Jahe



Gambar 4. Maserasi Jahe dengan larutan Etanol 70% selama 4 hari

bar 5. Penyaringan Jahe setelah Maserasi



Gambar 6. Pencampuran Ekstrak Jahe dan Madu

Gambar 7. Produk Ginger Honey

Gambar 8. Madu Trigona *sp* Sebagai Campuran Ekstrak Jahe

Proses Pengambilan Darah *Pretest* dan *Posttest*

Gambar 9. Pengambilan Darah

Gambar 10. Proses Peningkatan Kondisi Stress

Proses Pemberian Intervensi

Gambar 11. Pemberian Intervensi Ginger Honey

Perhitungan Dosis Ginger Honey

Berdasarkan penelitian Azman *et. al* (2016) dosis lazim pemberian madu tualang pada tikus sebanyak 200 mg per hari memiliki pengaruh terhadap penurunan kadar kortikosteron.

Dosis = Dosis lazim x faktor konversi
= 200 mg x 0,14
= 28 mg/20g BB

Jika bobot mencit 30 gram
= (30/20) x 28
= 1.5 x 28
= 42 mg
= 0.042 gram
= 0.04 ml

Jadi, masing-masing mencit mendapatkan dosis *ginger honey* sebanyak 0.04 ml kemudian diencerkan sebanyak 5 kali dengan *aquadest* menjadi 0,2 ml.

Tabel Faktor Konversi

	Mencit 20 gr	Tikus 200 gr	Marmot 400 gr	Kelinci 1,5 kg	Kucing 2 kg	Kera 4 kg	Anjing 12 kg	Manusia 70 kg
Mencit 20 gr	1.0	7.0	12.25	27.8	29.7	64.1	124.2	387.9
Tikus 200 gr	0.14	1.0	1.74	3.9	4.2	9.2	17.8	56.0
Marmot 400 gr	0.08	0.57	1.0	2.25	2.4	5.2	10.2	31.5
Kelinci 1,5 kg	0.04	0.25	0.44	1.0	1.08	2.4	4.5	14.2
Kucing 2 kg	0.03	0.23	0.41	0.92	1.0	2.2	4.1	13.0
Kera 4 kg	0.016	0.11	0.19	0.42	0.45	1.0	1.9	6.1
Anjing 12 kg	0.008	0.06	0.1	0.22	0.24	0.52	1.0	3.1
Manusia 70 kg	0.0026	0.018	0.031	0.07	0.076	0.16	0.32	1.0

(Sumber: Laurence & Bacharach, 1964)

Bobot Badan Mencit Selama Intervensi

KELOMPOK	HARI					
	Ke 1	Ke 3	Ke 6	Ke 9	Ke 12	Ke 15
Bobot Badan Mencit (g) untuk *Ginger Honey*						
1	26	26	26	27	27	27
2	25	26	26	27	27	27
3	20	20	25	25	26	27
4	27	27	31	31	31	31
5	21	21	22	23	24	24
Bobot Badan Mencit (g) untuk Kontrol						
1	26	25	25	24	24	24
2	27	27	26	26	24	24
3	26	26	24	23	23	22
4	28	27	27	27	24	24
5	25	24	23	23	22	22

Tabel Indikator Stres

Kelompok	M	S	Hari Intervensi													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Kontrol	1	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	2	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	3	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	4	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	5	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Ginger Honey	1	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	2	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	3	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	4	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	5	A	√	√	√	√	√	√	√	√	√	√	√	√	√	√
		B	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Keterangan :

= Mencit ke-

= Tanda-tanda stres

A = Jika mencit mempertahankan posisi hidung tetap berada di atas air

B = Jika mencit telah mengapung di atas air tanpa melakukan banyak pergerakan

Tabel Kadar Kortisol, Estrogen, dan Glutathione

1. Tabel Kadar Kortisol *Pretest* dan *Posttest*

GH_PreKor	Con_PreKor	GH_PostKor	Con_PostKor
8.907	8.9178	7.6573	12.1116
7.9777	8.3132	6.6009	17.0406
10.6153	7.721	9.5212	9.2396
9.5601	7.5423	7.6061	9.8565
8.847	7.6531	7.6031	9.1527

2. Tabel Kadar Estradiol *Pretest* dan *Posttest*

GH_PreEst	Con_PreEst	GH_PostEst	Con_PostEst
9.7941	2.1835	26.8116	11.3896
17.646	3.2076	31.8116	10.0965
14.0757	1.2443	29.0016	2.1835
8.5155	1.2443	25.1906	3.2353
9.3256	3.3877	31.6793	2.3544

3. Tabel Kadar Gluthatione *Pretest* dan *Posttest*

GH_PreGlu	Con_PreGlu	GH_PostGlu	Con_PostGlu
.7186	.5099	1.1822	1.2770
.4917	.3527	.7444	.0446
.4624	1.1308	.7276	.7755
.1313	2.2840	.8605	1.8534
.3476	.6532	.8766	.2377

Uji Statistik

1. Kelompok Ginger Honey pada Kadar Kortisol

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	GH_PreKor	9.181420	5	.9792210	.4379210
	GH_PostKor	7.797720	5	1.0603153	.4741874
Pair 2	Con_PreKor	8.029480	5	.5796067	.2592080
	Con_PostKor	11.480200	5	3.3313158	1.4898097

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	GH_PreKor - GH_PostKor	1.3837000	.3341623	.1494419	.9687826	1.7986174	9.259	4	.001
Pair 2	Con_PreKor - Con_PostKor	-3.4507200	3.0307175	1.3553781	-7.2138528	.3124128	-2.546	4	.064

2. Kelompok Ginger Honey Pada Kadar Estrogen

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	GH_PreEst	11.871380	5	3.8814714	1.7358468
	GH_PostEst	28.898940	5	2.9297313	1.3102157
Pair 2	Con_PreEst	2.253480	5	1.0293913	.4603578
	Con_PostEst	5.851860	5	4.5060795	2.0151800

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	GH_PreEst - GH_PostEst	-17.0275600	3.2054597	1.4335251	-21.0076639	-13.0474562	-11.878	4	.000
Pair 2	Con_PreEst - Con_PostEst	-3.5983800	4.2831476	1.9154818	-8.9166102	1.7198502	-1.879	4	.134

3. Kelompok Ginger Honey Pada Kadar Gluthathione

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	GH_PreGlu	.430320	5	.2145679	.0959577
	GH_PostGlu	.878260	5	.1825614	.0816439
Pair 2	Con_PreGlu	.986120	5	.7817076	.3495903
	Con_PostGlu	.837640	5	.7445649	.3329795

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
					95% Confidence Interval of the Difference				
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper			
Pair 1	GH_PreGlu - GH_PostGlu	-.4479400	.1983908	.0887231	-.6942748	-.2016052	-5.049	4	.007
Pair 2	Con_PreGlu - Con_PostGlu	.1484800	.5141574	.2299382	-.4899307	.7868907	.646	4	.554

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THE POTENTIALS OF GINGER HONEY AS A SUPPLEMENT FOR PRECONCEPTION WOMEN WITH MILD STRESS

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ABSTRACT

Background: Stressful conditions in preconception women characterized by the increased levels of the cortisol hormone can cause a state of oxidative stress. Imbalance of antioxidants and free radicals will make the body has a state of oxidative stress and disruption of the endocrine system. PCOS, irregular menstrual cycle, decreased oocyte quality, and infertility result from stressful conditions and oxidative stress.
Objective: This study aimed to determine the effect of ginger honey supplementation on decreasing cortisol hormone levels, increasing glutathione levels, and increasing estrogen levels.
Method: this study was an in vivo laboratory research and conducted in the Bio pharmacy Laboratory, and the Microbiology Laboratory of the Teaching Hospital of Hasanuddin University. Pretest-posttest control group design. This study sample is 2-3 months female Balb/c mice divided into Group 1 as the negative control and group 2 as ginger honey as much as 28 mg/20 g BW for 14 days. The evaluations of cortisol hormone levels, glutathione levels, and estrogen hormones conducted using the ELISA method.
Results: the data are analyzed using paired T-tests. The administration of ginger honey significantly ($p<0.05$) is able to reduce cortisol levels ($p=0.001$) by -1.383 ng/ml, increases glutathione levels ($p=0.007$) by 0.447 ng/ml, and increases estrogen hormone levels ($p=0.001$) of 17,027 ng/ml.
Conclusion: Ginger honey affects reducing cortisol levels, increasing glutathione, and estrogen levels. Ginger honey supplements can be used as complementary therapies in midwifery for preconception women who experience mild stress.

Keywords: Cortisol; *Ginger Honey*; Glutathione; Estrogen; Stress, Oxidative Stress

Introduction

Preconception care is a supply intervention given to women and their couples before the conception to improve women's and children's health in the long term and short term (WHO, 2013). The significant ways to improve the quality of preconception women are to improve nutritional status and improve their lifestyle (Stephenson, 2018).

Nutrition is associated with obesity and underweight conditions that are influenced by stressful situations, which cause an increase in the cortisol hormone as a physiological response to stress that is secreted by the adrenal cortex (Aschbacher *et al.*, 2013; Lee, Kim and Choi, 2015; Wiegner *et al.*, 2015). During menstruation, pregnancy, childbirth, postpartum, and menopause, working women are more likely to experience stress up to two times more than men (Albert, 2015; Wiegner *et al.*, 2015; Nejad *et al.*, 2016). Oxidative stress is a state of imbalance between reactive oxygen species (ROS) and biological systems' ability to reduce ROS levels (Annamalay, 2018). These conditions can cause some reproductive diseases such as endometriosis, PCOS, decreased oocyte quality, infertility, miscarriage, preeclampsia, IUGR, and premature birth (Yuslianti *et al.*, 2015; Duhig, Chappell and Shennan, 2016) occurrence of Polycystic Ovarian Syndrome (PCOS), while the PCOS associated with reproductive and metabolic diseases. It is a condition that can characterize by irregular menstruation, oligomenorrhea or amenorrhea, and anovulation (Mohammadi, 2019).

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. Fetal growth inhibited due to excessive exposure to glucocorticoid hormones (Zelena, 2015). Oxidative stress correlated to many patterns of disease (Khoubnasab Jafari, Ansarin and Jouyban, 2015). The body's main antioxidant, glutathione, has an important role in preventing cell damage caused by oxidative stress (Kwon *et al.*, 2019). It can also maintain vitamin C and vitamin E, which also acts as exogenous antioxidants (Ahmed *et al.*, 2018).

Low levels of estrogen and stressful conditions also trigger women to be vulnerable to oxidative stress. Previous studies have suggested that high corticosterone levels are associated with low estradiol and hurt mood (Al-Rahbi *et al.*, 2014). While the low estrogen levels leading to amenorrhea and irregular menstruation (Ranabil and Reetu, 2011). Young women and menopausal women who experience decreased estrogen are more at risk for autoimmune disease (Assad *et al.*, 2017)

The provision of ginger containing antioxidants can reduce oxidation activity (Eissa *et al.*, 2017), and the ethanol content of ginger increases enzymatic antioxidant activity (Ighodaro and Akinloye, 2018). Ginger can also replace the role of mefenamic acid (NSAIDs) in reducing menstrual pain in women (Azman *et al.*, 2018)

Honey with antioxidant content such as flavonoids, phenolic acids, enzymes, vitamins (A, E, C) (Khalil, Sulaiman and Boukraa, 2010), and a little mineral (copper and iron) (Chua *et al.*, 2013)) can prevent cancer, heart disease, infectious diseases, decreased neurological function, inflammation and aging (Khalil, Sulaiman and Boukraa, 2010). Honey administration to 2 months mice affects brain development and memory and reduces the anxiety Mijanur Rahman, Gan and Khalil, 2014). Administration of Tualang honey in induced stress TH and corticosterone levels, reduce MDA, and increase antioxidant activity in the brain

Method

Design

This research is an in vivo laboratory research and 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. The sample of this study was female Balb / c mice with the age of 2-3 months, which divided into two groups (5 of each group). Group 1 as a control group as a standard feed, and group 2 as ginger honey (a mixture of 10 mg of *trigona spp* honey and 20 mg of ginger) as much as 28 mg / 20 g BW is given by gavage for 14 days. Before administering the intervention, the mice will be given swimming treatment for 15 minutes to increase the stress state. The examination of cortisol hormone levels, glutathione levels, and estrogen hormone levels carried out using the ELISA method on the 14th day.

Ethics Considerations

The Ethics Committee approved this research of Faculty of Medicine, Universitas Hasanuddin

Result

In the research that has been carried out, the result is a change in body weight in female Balb/c mice in each group and is displayed in tabular form, as follow

Table 1: Changes in Balb/c Female Mice Body Weight in the Ginger Honey Group and Control Group

Days	Changes in Balb/c Female Mouse Body Weight	
	Control	*Ginger Honey* *Mean ± SD*
Day 1	26,40	23,80
Day 3	25,80	24,00
Day 6	25,00	26,00
Day 9	24,60	26,60
Day 12	23,40	26,80
Day 15	23,20	27,20

Table 1 shows the changes in mice weights in the Ginger honey intervention group from day 1 to day 15 compared to the control group who lost weight

Table 2: Analysis of Cortisol Hormone Levels in Each Group

Time	Cortisol Level (ng/ml)	
	Control	*Ginger Honey* *Mean ± SD*
Pre	8,029 ± 0,579	9,265 ± 1,109
Post	11,480 ± 3.331	7,846 ± 1,217
Different Mean	+ 3,450	-1,383
**p* value	0,064	0,001

*Paired T-test

the results of the statistical analysis of the paired T-test show a significant value (p<0.001)

roup on the results of the cortisol hormone analysis of female mice Balb / c (p = 0.005)

Table 3: Analysis of Glutathione Hormone Level in Each Group

Time	Glutathione Hormone Level(ng/ml)	
	Control	*Ginger Honey* Mean ± SD
Pre	0,986 ± 0,781	0,430 ± 0,214
Post	0,837 ± 0,744	0,878 ± 0,182
Different Mean	-0,148	0,447
*p value	0,554	0,007

**Paired T-test*

Table 3 shows the results of paired T-test data in the ginger honey group and the control group. There are some differences in elevation levels of glutathione in the intervention group and the control group. There is a significant increase ($p < 0.05$) in the ginger honey intervention group by 0.427 ng/ml ($p = 0.007$)

Table 4: Analysis of Estrogen Hormone Level in Each Group

Time	Estrogen Hormone Level (ng/ml)	
	Control	*Ginger Honey* Mean ± SD
Pre	2,253 ± 1,029	11,871 ± 3,881
Post	5,851 ± 4,506	28,898 ± 2,929
Different Mean	3,598	17,027
*p value	0,134	0,001

**Paired T-test*

Table 4 shows estrogen levels of Balb / c female mice in the control group and intervention group results from the analysis of the paired T-test are in a significant value of $p < 0.05$. The table shows a significant increase in estrogen levels of 17,027 ng/ml ($p=0.001$) compared to the control group which increased by 3,598 ng/ml ($p=0.134$)

Table 5: Differences in Cortisol Hormone Levels, Glutathione and Estrogen Hormone Levels Before and After Intervention in Balb/c Female Mice in the negative control group

Time	*Control Group*		
	Cortisol Hormone (ng/dL)	Glutathione Level (ng/dL)	Estrogen Hormone (ng/dL)
Pre	8,029 ± 0,579	0,986 ± 0,781	2.253 ± 1,029
Post	11,480 ± 3.331	0,837 ± 0,744	5.851 ± 4,506
Diff. Mean	+ 3,450	-0,148	3.598
**p-value*	0,064	0,554	0,134

**Paired T-test*

Table 5 shows cortisol, glutathione, and estrogen level in the control group, which only took standard feed during the intervention period in the intervention group. There is no significant change in the value of cortisol, ogen level of Balb/c female mice ($p<0,05$) after 14 days.

Table 6: 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 Level (ng/dL)	Estrogen Hormone (ng/dL)
Pre	9,265 ± 1,109	0,430 ± 0,214	11,871 ± 3,881
Post	7,846 ± 1,217	0,878 ± 0,182	28,898 ± 2,929
Diff Mean	-1,383	0,447	17,027
**p value*	0,001	0,007	0,001

**Paired T-test*

Based on the data of table 6, in the Intervention group, ginger honey had the most significant effect on decreasing cortisol level by -1,383 ng/ml and increasing estrogen level hormone by 17,027 ng/ml. Statistical analysis of the three indicators showed the highest significant value is on estrogen level, which is p=0,001 (17,027 ng/ml).

Discussion

Ginger honey as much as 28 mg/20 g BW in female Balb/c mice can reduce levels of the hormone cortisol as an indicator of stressful states by -1,383 ng/ml, increase glutathione levels by 0,447 ng/ml as antioxidants that handle oxidative stress status, and increase levels of estrogen hormone of 17,027 ng/ml to prevent female reproductive health problems due to low estrogen in the body

Excessive physical activities in women can increase blood cortisol levels and interfere with the release of the hormone GnRH, which can prolong the follicular phase and shortening the luteal period in experimental animals due to an increase in ROS (Mosavat, Ooi and Mohamed, 2014). A mixture of honey and royal jelly given in high doses to male athletes can reduce hormone cortisol levels. On the other hand, it can cause an increase in the hormone testosterone (Büyükipekçi *et al.*, 2018). Ginger extract can reduce cholesterol levels and balance the hormones estrogen and progesterone in mice with PCOS, the content of gingerol polyphenols and flavonoids in the ginger act as antioxidants (Atashpour *et al.*, 2017). Another natural ingredient, ginger (*Zingiber officinale*) has been shown to significantly reduce LDL cholesterol, total cholesterol, and body weight after being given for three months as much as 5 mg/day in patients with hyperlipidemia (Murad, Niaz and Aslam, 2018). The line with this research that Ginger honey supplements can significantly reduce the hormone cortisol levels in female Balb / c mice by -1,383 ng/ml.

Glutathione exists in almost all body cells that act as antioxidants hydrogen donors to free radicals to prevent oxidative stress (Weschawalit *et al.*, 2017). Oxidative stress triggers PCO disease, oocyte damage, and infertility (Adeoye *et al.*, 2018). 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 (Abdul Sani *et al.*, shows the administration of ginger honey supplements can significantly increase glutathione . In a previous study on 12 Sprague Dawley rats given Gelam honey as much as 2.5 ml/kg BW 1 tsp for adults in 8 months can reduce levels of MDA and levels of DNA damage (Sahhugi, 014) Previous research also states that Rambutan Honey contains flavonoids and phenolic as which plays a role in reducing lipid peroxide and free radicals (Yuslianti *et al.*, 2015)

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 (Ranabil and Reetu, 2011). On the other hand, an increase in LH, testosterone due to metabolic disorders in the body, can cause a state of infertility due to ovulation abnormalities. The provision of ginger in mice with ovulation abnormalities can improve and balance the hormones LH, FSH, estrogen, and progesterone (Atashpour *et al.*, 2017). In this research shows 28 mg/20 g BW Ginger honey administration for 14 days increased estrogen levels by 17,027 ng/ml in induced stress Balb/c female mice statistically has a significant effect on decreasing cortisol hormone levels, increasing glutathione levels, and increasing levels of the hormone estrogen on. The most significant impact on these supplements is on the increase in estrogen levels.

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Conflict of Interest

The authors declare that there is no conflict of interest

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POTENSI *GINGER HONEY* SEBAGAI SUPLEMEN WANITA PRAKONSEPSI DENGAN STRES RINGAN MENGGUNAKAN MENCIT BETINA BALB/C SEBAGAI MEDIA INTERVENSI

THE POTENTIAL OF GINGER HONEY AS A SUPPLEMENT FOR PRACONCEPTION WOMEN WITH MILD STRESS USING BALB/c MICE AS INTERVENTION MEDIA

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