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Glucocorticoid and cortisol hormone in response to honey and honey propolis supplementation in mild stress women☆

Andi Nilawati Usman[a,*], **Andi Zulkifli Abdullah**[b], **Indah Raya**[c], **Budiaman Budiaman**[d], **Agussalim Bukhari**[e]

[a] *Midwifery Department, Graduated School, Hasanuddin University, Indonesia*
[b] *Epidemiology Department, Public Health, Hasanuddin University, Indonesia*
[c] *Chemistry Faculty, Hasanuddin University, Indonesia*
[d] *Agriculture Department, Hasanuddin University, Indonesia*
[e] *Medicine Faculty, Hasanuddin University, Indonesia*

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Abstract
Objective: This study aimed to assess the response of supplementation of honey and honey propolis to women who experience mild stress.
Methods: The subjects of 30 people were divided into 3 groups; control, honey, and propolis honey every 10 people per group. All groups were given the same dose of 60 g/day for 14 days. Measurements of glucocorticoid and cortisol hormones using Enzyme-Linked Immunosorbent Assay (ELISA) and the difference in cortisol hormone levels before and after the intervention were analyzed by a paired *T*-test.
Results: Honey and propolis honey group decrease cortisol levels but none of the groups have significant changes. This is reciprocal with the changes in the hormone cortisol, the decrease in glucocorticoid hormone levels in the group given honey is the highest following propolis honey and the control group. However, changes in glucocorticoid hormones in the honey group were statistically significant.
Conclusion: Our result confirmed that in women who experience mild stress, honey and honey propolis have the potential to reduce stress-related hormones, that is glucocorticoids and cortisol, this reduction does not have the potential to suppress the immune system.

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* Corresponding author.
E-mail address: andinilawati@pasca.unhas.ac.id (A.N. Usman).

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Introduction

Women are vulnerable to psychosocial stressors and become more susceptible to cardiovascular disease.[1] Cortisol will increase if there are unbalanced mental conditions such as anxiety, stress or depression. The increase in cortisol is one mechanism that maintains the use of energy and controls blood pressure but high and long-lasting secretions implicated to cortisol dysfunction and becomes proinflammatory.[2] Intervention to reduce cortisol but not conduce dysfunction is needed.

Stress also increases glucocorticoids that have a pivotal role in inflammation and the immune system, it will prevent the production of inflammatory mediators and helps adapt to stress.[3] Long-term increases in glucocorticoid hormones have an adverse effect, they can interfere with neuronal function and lead to the occurrence of glucocorticoid hormone resistance.[4]

Recently, developing Nutritional Psychiatry is how a person's diet will prevent or reduce mental or psychological disorders such as depression, anxiety, stress. This research continues to investigate the efficacy of various studies that have been conducted.[5] This research continues to investigate the efficacy of various studies that have been conducted. Honey is a bee product used as a supplement and very acceptable to the community.

Published studies have shown that honey supplementation has an effect on hormones associated with stress, although studies are still in experimental animals the publication about this is still lacking.[6] The latest mechanism suggested is antioxidants or foods containing flavonoids could relieve stress and mental disorders through oxidative stress pathways. This can be explained by the function of antioxidants eliminate oxygen reactive species (ROS) and reactive nitrogen species (RNS), then damage to neurons will be protected in the brain, it is expected to prevent depression and symptoms such as anxiety.[7] This study supplements local honey in South Sulawesi, Indonesia in women who experience mild stress to see the cortisol and glucocorticoid hormone responses that occur.

Method

Honey and honey propolis

The honey used in this study was local honey from the district of Gowa, South Sulawesi, a district in Indonesia (the honey content is described in Table 1). This honey was processed by depositing it for 7 days in 3 different containers and then examined in the laboratory the contents of fungi, bacteria *Escherichia coli* and *Salmonella typhi*. After ensuring honey was free of fungi, *E. coli* and *Salmonella typhi*, honey is included in glass bottles with a volume of 330 g per bottle.

Propolis honey is made by mixing 85% of honey and 15% propolis (water extract), propolis extract based on the procedure from FAO, the honey content of propolis has been tested and published {Usman, 2016 #3}. After ensuring the honey is free of fungi, *E. coli* and Salmonella typhi, honey is included in glass bottles with a volume of 330 g per bottle.

Subjects

We conducted an experimental study that included 30 mild stressed women screened with the Depression questionnaire, Anxiety and Stress Scales (DASS). Ethical permission has been obtained from the ethics committee of the Public Health Faculty and Medicine Faculty of the Hasanuddin University. All subjects were given informed consent before being included in the study. All subjects were asked not to take any supplements and not to implement a different type of diet from their daily life before being included in the study. Each group consisted of 10 subjects and no one dropped out during the study.

Experimental design

It was an experimental study with a pre-post study design. Subjects were randomly allocated to three groups: control group, the control group obtained placebo, honey-like liquid with the same dose as the intervention group 60 g/day, the honey group received 60 g of honey/day and honey propolis group which also received propolis honey 60 g/day.

The study lasted for 14 days, before and after the study (days 0 and 15) vein blood samples were taken as much as 5 ml and directly centrifuged to eliminate plasma and serum. Every week a personal visit was held to remind adherents to the research protocol and to provide short message service for questions at any time.

Hormone analysis

Cortisol and glucocorticoid hormones were analyzed using Enzyme-Linked Immunosorbent Assay (ELISA). Human ELISA kit for the hormone cortisol uses the Diagnostic Biochem Canada (DBC) product while the human glucocorticoid ELISA kit uses Bioassay Technology Laboratory. The sample analysis and extraction procedure follow the product instructions.

Result

Data shows that the characteristics of age, education, and employment also body weight, blood glucose, total cholesterol and blood pressure among the control groups, and the intervention almost similar (Table 1).

The results of the analysis showed that the intervention group given honey had the highest decrease (3.250 μg/dl) in cortisol levels compared to the others and the control group had the lowest decrease (0.626 μg/dl) in cortisol levels. Although the honey group and propolis honey group both observed a decrease in cortisol levels, none of the groups experienced significant changes ($P > 0.05$) (Table 2).

The results of the analysis are reciprocal with the decreasing of the cortisol hormone, the decrease in glucocorticoid hormone levels in the group given honey was the highest (7.664 μg/dl), and statistically significant ($P < 0.05$) (Table 3).

Table 1 Characteristics of respondents.

Characteristics	Group		
	Control ($n = 10$)	Honey ($n = 10$)	Honey propolis ($n = 10$)
Age Mean (year)	30.45	30.15	30.75
Education n (%)			
High school	4 (13.33)	4 (13.33)	4 (13.33)
Bachelor	6 (20.00)	6 (20.00)	6 (20.00)
Occupation n (%)			
Housewife	5 (16.67)	6 (20.00)	5 (16.67)
Government employee	5 (16.67)	4 (13.33)	5 (16.67)
Body weight Mean (kg)	51.65	50.89	50.94
Blood glucose Mean (mg/dl)	94.0	100.15	99.0
Total cholesterol Mean (mg/dl)	150.63	160.17	150.10
Blood pressure Mean (mmHg)			
Systolic	128.20	130.68	120.89
Diastolic	85.00	87.00	80.00

Table 2 Cortisol hormones before and after interventions.

Group	Cortisol hormone levels Mean ± SD (μg/dl)		Differences in cortisol levels before and after intervention (μg/dl)	*P*-value
	Before intervention	After intervention		
Control	17.650 ± 5.770	17.024 ± 3.873	0.626	0.959[a]
Honey	17.429 ± 5.678	14.179 ± 2.774	3.250	0.114[a]
Honey propolis	15.477 ± 3.810	14.009 ± 4.138	1.468	0.385[a]

[a] Paired sample *T*-test.

Table 3 Cortisol hormones before and after interventions.

Group	Level of hormone glucocorticoid Mean ± SD (ng/ml)		Differences in glucocorticoid levels before and after intervention (μg/dl)	*P*-value
	Before intervention	After intervention		
Control	66.168 ± 13.825	64.673 ± 7.897	1.495	0.760[a]
Honey	71.999 ± 12.615	64.335 ± 5.728	7.664	0.049[a]
Honey propolis	48.459 ± 7.393	47.866 ± 5.399	0.593	0.809[a]

[a] Paired sample *T*-test.

Discussion

The intervention group tended to decrease in cortisol levels but was not significant, this was allegedly associated with shorter intervention times (15 days), the time needed longer intervention. However, the administration of honey could significantly reduce glucocorticoid levels, another assumption is all women included are those who experience mild stress and the range of cortisol levels is still be considered normal. This study does not prove that honey and honey propolis could reduce cortisol and glucocorticoid but rather in an effort to balance in the human body so that the dose given in mild stress conditions in this study is appropriate because it will not be immunosuppressed.

Research that intervenes honey and propolis honey in stress cases is still very lacking. The study of honey in induced animal models for stress shows that honey could reduce oxidative stress in the brain so that it can improve memory lost due to stress and honey is considered to have effects such as anti-depressant.[8] A study showed that propolis made in the form of an essential oil succeeded in reducing plasma cortisol levels.[9]

The latest therapeutic target in the case of neuropsychiatry disorders does not seem to be something that can have a therapeutic effect but can also normalize damage to the brain due to oxidative stress.[9] An increase in stress oxidative biomarkers is reciprocal with an increase in cortisol and thus also shows that evidence is of the importance of redu-

cing and eliminating oxidative stress in the body to deal with stress.[10] Provision of antioxidants is also proven to be able to reduce stress hormones and honey and honey propolis is one candidate supplement that can have antidepressant effects without causing pressure on the immune system.[10–12]

Conclusions

Our result confirmed that in women who experience mild stress, honey and honey propolis have the potential to reduce stress-related hormones, namely glucocorticoids and cortisol but this reduction does not have the potential to suppress the immune system.

Conflict of interest

The authors declare no conflict of interest.

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