DOI: 10.17354/ijpphs/2016/43

Original Article

Effect Red Guava Juice (*Psidium guajava* L) on Blood Glucose Levels Fasting Wistar Rats Induced Pre-diabetes Dexamethasone

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ABSTRACT

Background: Pre-diabetes is a condition where blood glucose levels are higher than normal but not high enough to say diabetes, and it can develop into diabetes mellitus type 2, two conditions associated with pre-diabetes are impaired glucose tolerance or fasting blood glucose (FBG) disturbed. The purpose of this study was to determine the effect of red guava juice (*Psidium guajava* L) which is a source of antioxidants on FBG levels Wistar rat strain.

Materials and Methods: This research is true experimental design of randomized pre- and post-test with control group design, in which the experimental group was divided into five groups: Control group negative given only the standard feed and drinking water *ad libitum*, positive control induced with dexamethasone, and three treatment groups by the addition of red guava juice at a dose of 3.6, 7.2, and 10.8 g/head/day given orally. The study was conducted over a period of 3 weeks. Blood glucose levels were taken during pre-treatment for the control and treatment groups, whereas post-treatment for all three treatment groups only, then the data are collected after it is processed using one-way ANOVA statistical test with a confidence level of 95%.

Results: The results of this study are dexamethasone improving FBG levels pre-treatment, and post-FBG levels in the treatment group were given red guava juice all decreased.

Conclusion: The conclusion of this study is a red guava juice can lower FBG levels in mice pre-diabetes.

Key words: Pre-diabetes, Glucose fasting, Dexamethasone, Red guava juice, Rats

INTRODUCTION

Pre-diabetes is a condition where blood glucose levels are higher than normal but not high enough to say diabetes, and it can develop into diabetes mellitus (DM) type 2, two conditions associated with pre-diabetes are impaired glucose tolerance or fasting blood glucose (FBG) disturbed.[1]

Pre-diabetes has become a pandemic with a higher prevalence of diabetes; the prevalence of diabetes in the United States was 24.1 million while 57 million people have pre-diabetes. In 2030, the International Diabetes Federation predicts that 398 million people worldwide are experiencing pre-diabetes and 175 million of them have not been diagnosed so that it can develop into diabetes unnoticed and prevention.[2]

Pre-diabetes is associated with a diet high in fats and carbohydrates and low in fiber which can lead to obesity and is associated with increased blood glucose due to insulin resistance. In the process of carbohydrate metabolism, insulin plays an important role in getting glucose into cells which will then be used as energy. When insulin resistance occurs, the glucose cannot enters into cells and remains in the blood vessels so that the levels of glucose in the blood will increase.[3]

Insulin resistance may be due to oxidative stress as a result of reactive oxygen species (ROS) formed during glycation and oxidation of lipids and glucose. One compound that is capable of controlling the formation of ROS is an antioxidant. Oxidative stress is a state of balance between free radicals and

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Submission: 09-2016; Peer Review: 10-2016; Acceptance: 11-2016; Publishing: 12-2016

antioxidant systems. The mechanism of antioxidants in lowering blood glucose levels is through inhibition of ROS, process improvement gluconeogenesis, inhibit aldose reductase enzyme activity, stimulates the secretion of insulin by the beta cells, and increase the activity of the enzyme hexokinase. Oxidative stress pre-diabetes will accelerate the onset of DM through the metabolism of glucose and free fatty acid overload.[4]

Red guava fruit (*Psidium guajava* L) is a plant that can be used as a source of antioxidants. Vitamin C content results in guava 87 mg/100 g higher than the orange contains 49 mg/100 g. In addition, Phytochemical compounds contained in guava are a saponin, essential oil, flavonoid, and polyphenol compounds.[5] The composition of the natural antioxidant flavonoids and Vitamin C can prevent the formation of free radicals in the body or as an antioxidant and antidiabetic.[6] Vitamin C has a correlation with the antioxidant activity of flavonoids found in guava, i.e., the higher the Vitamin C, the antioxidant activity of flavonoids higher.

Based on the above, the purpose of this study was to determine the effect of guava juice (*Psidium guajava* L) which is a source of antioxidants on FBG levels Wistar rat strain.

MATERIALS AND METHODS

This type of research is true experimental design of randomized pre- and post-test with control group design, which allows researchers to measure the effect of treatment (intervention) in the experimental group by comparing the experimental group and control group. There are two control and three treatment groups.

This research was conducted in July 2016, to take for 3 weeks, with 1 week for the stage adaptation, 5 days for giving dexamethasone to the positive control group (P1) and three treatment groups (P2, P3, and P4), and 9 days award red guava juice (*Psidium guajava* L) to three treatment groups. Research conducted at the Laboratory of the Faculty of Medicine, University of Airlangga.

The sample size used in this study was 30 Wistar strain male rats were divided into five groups: The first negative control group fed standard and water *ad libitum*, the second is the positive control group fed standard and water *ad libitum* with the induction of dexamethasone 0.6 mg/day, the third is a P2 group: The group given standard feed and drinking water *ad libitum* induced dexamethasone 0.6 mg/head/day with the addition of red guava juice at a dose of 3.6 g/tail/day, Fourth P3 group, namely the group given standard feed and drinking water *ad libitum* induced dexamethasone 0.6 mg/day with the addition of red guava juice at a dose of 7.2 g/head/day, and the fifth group is P4: Group fed standard and drinking water *ad libitum* induced dexamethasone 0.6 mg/head/day with the addition of red guava juice at a dose of 10.8 g/head/day.

Criteria for inclusion in this study are using male Wistar strain rats, aged 2-3 months, weighing rats 150-200 g as well as healthy mice in the circumstances while exclusion criteria were rats experience pain or death during the study.

The Data of fasting blood glucose levels for the negative control group, positive control group and three treatment groups were taken at the same time in the fifth day of study. which the fasting blood glucoseof treatment group is taken before red guava juice were given. The Blood of lateral veins was collected , where the analysis of blood glucose levels using a glucose kit. While the three treatment groups, FBG levels taken at post-treatment with a blood sample on the intracardiac (heart), the analysis using calorimetric method.

After all the data are collected, then analyzed the data using one-way ANOVA test with a confidence level of 95%, followed by *post hoc* test using LSD.

RESULTS

Fasting Blood Glucose Pre-treatment

Mean FBG pre-test (before treatment) on male Wistar strain rats on each group can be seen in Table 1.

Mean FBG levels pre-test is highest in the group given standard feed with the addition of red guava juice 3.6 g (P2), amounting to 163.20 ± 13.14 mg/dL, and the mean FBG levels were lowest in the control group amounted to 121.00 ± 5.899 mg/dL as presented in Figure 1.

Different tests result mean FBG levels pre-test between the control group and the treatment group performed using one-way ANOVA test with a confidence level of 95% was obtained *P* value of 0.000, which means that there are at least a pair of groups that have differences between the mean FBG levels. To determine which group a couple different then test one-way ANOVA followed by *post hoc* test using LSD. Data of couples, where different groups to mean FBG levels pre-test, can be seen in Table 2.

Table 2 shows the differences in mean FBG levels pre-test (before treatment) between the control group (P0) with each treatment group are given a standard feed with a positive control (P1), red guava juice 3.6 g/tail/day (P2), red guava juice 7.2 g/head/day (P3) as well as red guava juice 10.8 g/head/day (P4).

Table 1: Mean fasting blood glucose (mg/dL) pre-treatment in the control group and the treatment group

Groups	Mean±SD	Minimum	Maximum
Negative control groups (P0)	121.00±5.899	114	130
Positive control groups (P1)	158.80±16.43	146	185
Red guava juice group 3.6 g (P2)	163.20±13.14	150	182
Red guava juice group 7.2 g (P3)	156.20±10.59	148	173
Red guava juice group 10.8 g (P4)	156.00±8.215	146	165

SD: Standard deviation

Table 2: Test difference fasting blood glucose pre-treatment between negative control group with treatment group

Group	*P*
Negative control group (P0) and positive control group (P1)	0.000
Negative control group (P0) and red guava juice group 3.6 g/head/day (P2)	0.000
Negative control group (P0) and red guava juice group 7.2 g/head/day (P3)	0.000
Negative control group (P0) and group of red guava juice 10.8 g/head/day (P4)	0.000

Data mean FBG levels pre-test (before treatment) between the positive control group and the treatment group was given red guava juice for 14 days showed no significant difference as shown in Table 3.

Fasting Blood Glucose Levels Post-treatment

Mean FBG post-test on male rats Wistar strain on each group can be seen in Table 4.

The mean levels of FBG post the lowest test contained in the group given standard feed with the addition of red guava juice 7.2 g (P3), which amounted to 87,000 ± 11.24 mg/dL, which is illustrated in Figure 2.

Differences in FBG levels post-test between the control group and the treatment group performed one-way ANOVA test with a confidence level of 95% was obtained *P* value of 0.000, which means that there are at least a pair of groups that have differences between the mean FBG levels. To determine which group a couple different then test one-way ANOVA followed by *post hoc* test using LSD.

Data of couples, where different groups to mean FBG levels post-test, can be seen in Table 5.

The result of the difference between the positive control group and the treatment group is shown in Table 6.

DISCUSSION

The mean FBG levels between the negative control group and positive control group showed no significant difference. This is due to glucocorticoid drugs can result in hyperglycemia. Hyperglycemia is an increase in blood glucose levels caused by excessive gluconeogenesis and can also be caused by the effects of insulin are inadequate. Increased blood glucose levels caused by excessive gluconeogenesis because the breakdown of amino acids and glycerol is converted into glucose, so the body will have an excess of glucose. When this condition occurred in a long time can result in insulin resistance.[7] Dexamethasone is a class of synthetic glucocorticoid class of steroid class of

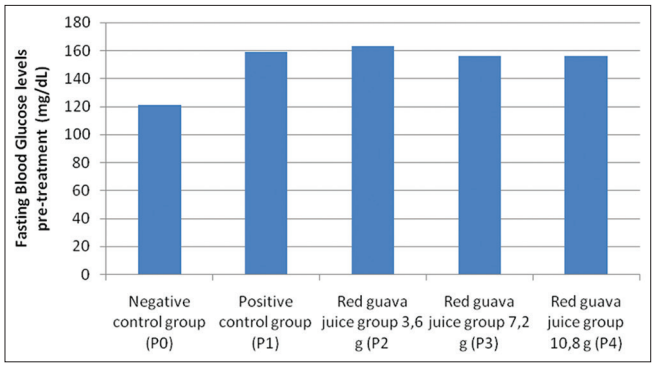

Figure 1: Average blood glucose fasting pre-treatment rats Wistar strain

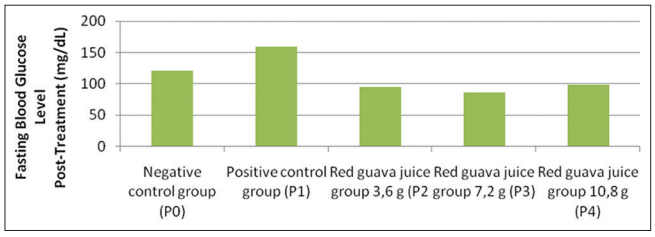

Figure 2: Mean fasting blood glucose post-treatment rats Wistar strain

Table 3: Test difference fasting blood glucose between pre-treatment group positive control and treatment group

Group	*P*
Positive control group (P1) and red guava juice group 3.6 g/head/day (P2)	0.551
Positive control group (P1) and red guava juice group 7.2 g/head/day (P3)	0.724
Positive control group (P1) and group of red guava juice 10.8 g/head/day (P4)	0.704
Red guava juice group 3.6 g (P2) and red guava juice group 7.2 g/head/day (P3)	0.346
Red guava juice group 3.6 g (P2) and group of red guava juice 10.8 g/head/day (P4)	0.333
Red guava juice group 7.2 g (P3) and group of red guava juice 10.8 g/head/day (P4)	0.978

Table 4: Mean fasting blood glucose (mg/dL) post-treatment between control group and the treatment group

Group	Mean±SD	Minimum	Maximum
Negative control groups (P0)	121.00±5.899	114	130
Positive control groups (P1)	158.80±16.43	146	185
Red guava juice group 3.6 g (P2)	95.000±17.84	72	113
Red guava juice group 7.2 g (P3)	87.000±11.24	75	101
Red guava juice group 10.8 g (P4)	99.000±16.00	74	113

SD: Standard deviation

Table 5: Test difference fasting blood glucose post-treatment between negative control group with treatment group

Group	*P*
Negative control group (P0) and positive control group (P1)	0.000
Negative control group (P0) and red guava juice group 3.6 g/head/day (P2)	0.008
Negative control group (P0) and red guava juice group 7.2 g/head/day (P3)	0.001
Negative control group (P0) and group of red guava juice 10.8 g/head/day (P4)	0.020

Table 6: Test difference fasting blood glucose between pre-treatment group positive control and treatment group

Group	*P*
Positive control group (P1) and red guava juice group 3.6 g/head/day (P2)	0.000
Positive control group (P1) and red guava juice group 7.2 g/head/day (P3)	0.000
Positive control group (P1) and group of red guava juice 10.8 g/head/day (P4)	0.000
Red guava juice group 3.6 g (P2) and red guava juice group 7.2 g/head/day (P3)	0.383
Red guava juice group 3.6 g (P2) and group of red guava juice 10.8 g/head/day (P4)	0.660
Red guava juice group 7.2 g (P3) and group of red guava juice 10.8 g/head/day (P4)	0.196

drugs which have anti-inflammatory and immunosuppressant. One effect of dexamethasone is increasing gluconeogenesis, namely the formation of glucose from protein thus increasing the risk of blood sugar.[8,7]

Hyperglycemia causes free redical auto-oxidation so as the occurrence of glucose, protein glycation, and activation of the metabolic pathway of polyol which further accelerates the formation of reactive oxygen compounds. The formation of reactive oxygen compounds that can improve the lipid modification, DNA, and proteins in different tissues. Molecular modifications in various tissues have resulted in an imbalance between the protective antioxidant (antioxidant defense) and increased production of free radicals. It was the beginning of oxidative damage known as oxidative stress.[9]

Other research suggests that controlling blood glucose levels back to normal is the best way that can be done to avoid the occurrence of DM.[10] There are various ways to control glucose levels in the blood, such as by pharmacological therapy and therapy with antioxidants. Pharmacological therapy has adverse effects such as kidney and liver damage if used for long periods of time. While antioxidant therapy assessed the ability of effective without side effects.

This study showed that the average FBG levels among the three treatment groups treated with red guava juice were not statistically significantly different, which means the lowest dose red guava juice is 3.6 g / day to the highest dose in the amount of 10.8 g / day can reduce fasting blood glucose levels wistar strain rats prediabetes.

Hyperglycemia in pre-diabetes causes increased oxidative stress and decreased antioxidant endogenous (produced by the body) so that the body requires exogenous antioxidants. Exogenous antioxidants can be obtained by increasing the intake of antioxidants such as Vitamin A, beta-carotene, Vitamin C, Vitamin E, polyphenols, flavonoids, isoflavones, and oleoresin. Antioxidant intake is protective against progression of pre-diabetes by inhibiting the peroxidation reactions that destroy pancreatic beta cells. The content of natural antioxidants is in the form of guava polyphenol compounds (flavonoids and phenolic). Some research suggests antioxidants administration of guava able to stabilize the free radical reactions and preventive.[11]

Red guava juice used in this study, first tested the content of flavonoids and Vitamin C, with results in 100 g of red guava contain 126.50 mg of Vitamin C and flavonoids of 85.52 mg.

Flavonoids may play a role in pancreatic tissue damage caused by alkylating DNA of induction drugs that can improve the morphology of the rat pancreas. Flavonoids are reported to have antidiabetic activity that is able to regenerate cells in the islets of Langerhans. Flavonoids are hypoglycemic by increasing gluconeogenesis, so there is no increase in glucose in the blood.[12]

The importance of Vitamin C for the regulation of blood sugar has been proven clinically. The study of 56 patients with pre-diabetes showed that administration of 2 g of Vitamin C per day can improve control of blood sugar levels. Doses of Vitamin C are recommended for patients with pre-diabetes and diabetes ranged from 1000 to 2000 mg/day, depending on individual circumstances. Vitamin C acts as an antioxidant that can reduce insulin resistance by improving endothelial function and decrease oxidative stress based on a study to prove that taking Vitamin C 1000 mg/day significantly lowered FBG levels.[13]

Vitamin C is an antioxidant that has an important role in the cell and plasma as an effective deterrent for many species of free radicals and also functions as reducing agent (electron donating) free radicals as well as disable it. Giving Vitamin C as an antioxidant to inhibit the oxidation process in the body so as to prevent the formation of free radicals and further cell damage.

CONCLUSION

The conclusion of this is award red guava juice with various doses can lower fasting blood glucose levels in prediabetes Wistar rats, so that both the lowest and highest doses effectively lower FBG levels.

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HOW TO CITE THIS ARTICLE:
Jasmani, Wirjatdmadi B, Adriani M. Effect Red Guava Juice (*Psidium guajava* L) on Blood Glucose Levels Fasting Wistar Rats Induced Pre-diabetes Dexamethasone. Int J Prevent Public Health Sci 2016;2(4):28-31.