C-26

LEMBAR
HASIL PENILAIAN SEJAWAT SEBIDANG ATAU *PEER REVIEW*
KARYA ILMIAH : PROSIDING

Judul Artikel Ilmiah	:	Effect Of Papaya Leaves Jelly On Reducing Blood Pressure In Prediabetic Women
Penulis Artikel Ilmiah	:	Syafira Noor Pratiwi, Choirun Nissa, Ahmad Syauqi, Hartanti Sandi Wijayanti, **Diana Nur Afifah**
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I. Hasil Penilaian *Peer Review* :

Komponen Yang Dinilai	Nilai Maksimal Jurnal Ilmiah (isikan di kolom yang sesuai)			Nilai Akhir Yang Diperoleh
	Seminar Internasional Terideks	Seminar Internasional Tidak Terideks	Seminar Nasional	
		15		
a. Kelengkapan dan Kesesuaian unsur isi jurnal (10%)		1,5		1,5
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c. Kecukupan dan kemutahiran data/informasi dan metodologi (30%)		4,5		4
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Nilai Total = (100%)		**15**		**14**
Nilai pengusul = **(40% x 14)/4 = 1,4**				

KOMENTAR/ULASAN PEER REVIEW		
Kelengkapan dan Kesesuaian Unsur	:	Prosiding dari seminar internasional dengan unsur lengkap dari abstract, introduction, methods, discussion, acknowledgement, dan references
Ruang Lingkup dan Kedalaman Pembahasan	:	Ruang lingkup peneitian masyarakat dengan desain intervensi papay jelly untuk mengetahui efeknya terhadap tekanan darah wanita pre-DM, sesuai bidang ilmu. Pembahasan mendalam dengan 25 referensi
Kecukupan & Kemutakhiran Data & Metodologi	:	Pembuatan papay jelly yang dapat dikonsumsi tanpa ada rasa pahit sehingga dapat diterima oleh responden selama intervensi
Kelengkapan Unsur dan Kualitas Penerbit	:	Terbitan lengkap memuat vol, tahun dan daftar isi dan ber-ISBN

Semarang, 14 Mei 2019
Penilai 1

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KOMENTAR/ULASAN PEER REVIEW		
Kelengkapan dan Kesesuaian Unsur	:	Prosiding internasional dari seminar internasional, ber-ISBN dengan unsur lengkap dari abstract hingga references
Ruang Lingkup dan Kedalaman Pembahasan	:	Ruang lingkup peneitian mengetahui pengaruh pemberian papay jelly terhadap tekanan darah wanita pre-DM, sesuai bidang ilmu. Pembahasan mendalam dengan 25 referensi
Kecukupan & Kemutakhiran Data & Metodologi	:	Penelitian true experiment design dengan pre-test post-test control group design.
Kelengkapan Unsur dan Kualitas Penerbit	:	Terbitan lengkap memuat vol, tahun dan daftar isi

Semarang, 11 Juli 2019
Penilai 2

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CONTENTS

Effect Of Papaya Leaves Jelly On Reducing Blood Pressure In Prediabetic Women

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ABSTRACT

Objective: Individual with prediabetes had higher risk of hypertension. In Indonesia, the prevalence of prediabetic with hypertension was higher than prediabetic with no hypertension. The chemical compounds contained in papaya leaves were known to have effects on lowering blood pressure. The purpose of this study was to assess the effect of papaya leaves jelly on blood pressure.
Methods: This was an experimental study with pre-post control group design. Subjects were 27 prediabetic women aged 35-50 years old which were divided into two groups. Treatment group (n = 13) received 24.6 grams papaya leaves jelly containing 182.4 mg chlorophyll, while the control group (n = 14) received jelly with green dye 24.6 grams. The interventions were performed for 20 days.
Results: Systolic and diastolic blood pressure in the treatment group had significant reduction from 130.14 ± 25.25 to 124.29 ± 25.48 (p = 0.008) and 89.00 ± 13.49 to 84.43 ± 14.16 (p = 0.02) respectively. Meanwhile, there was no significant blood pressure reduction in the control group.
Conclusion: Consumption of papaya leaves jelly could reduce systolic and diastolic blood pressure in prediabetic women.

Keywords: papaya leaves, blood pressure, prediabetic

INTRODUCTION

Prediabetes was a condition which blood glucose levels excess from normal levels but not higher than the criteria for people with diabetes mellitus.
Prediabetes individuals have fasting blood glucose levels between 100 mg/dl to 125 mg/dl and or have fasting glucose between 140 mg/dl to 199 mg/dl.

Prediabetic sufferers have a hypertensive risk of up to 2-3 times.[2] Based on Weili Xu research, prediabetes events were more common in women than in men.[3] Moreover, prediabetic women had a higher risk for having cardiovascular disease than prediabetic men because adiponectin levels in prediabetic women were lower than in prediabetic men.[4] Adiponectin was a hormone secreted by adipose tissue that had the following functions: 1) anti-diabetes by increasing insulin sensitivity; 2) anti-atherogenic by suppressing adhesion molecule expression; Enhancing the endothelial vasodilation effect, increasing the production of Nitric Oxide (NO).[4]

The risk of hypertension increased in individuals with prediabetes due to hyperglycemic that triggers oxidative stress and decreases superoxide dismutase (SOD).[5] High oxidative stress conditions could damage endothelial cells and inhibit the relaxation of blood vessels.[2] The state of hyperglycemy in the body could also disrupting the activity of NO as vasorelactor by relaxing the smooth muscle cells in the blood vessels.[5]

Prevention of the occurrence of diabetes and hypertension in patients with prediabetes should be done as early as possible. One way was to eat foods that contain antioxidant compounds that could balance the state of oxidative stress, in this case was SOD.[6]

SOD was antioxidant that produced in our body also exist in nature. SOD could be found in chlorophyll substances.[7] In addition to being able to act as SOD, chlorophyll content such as magnesium also had a positive effect on hypertension and diabetes. Magnesium could lowering blood pressure by lowering calcium levels that could lead to vasodilation.[8] Magnesium plays role in absorption of insulin-mediated glucose that could protect increasing risk of developing Type 2 Diabetes Mellitus (T2DM).[9]

Chlorophyll was found in leaves such as papaya leaves. Chlorophyll in papaya leaves was the highest chlorophyll content among cassava leaves, pegagan, spinach, cincau, kangkung and kemangi.[10] Papaya leaves were potential if used as functional food. However, papaya leaves have a weakness that was bitter taste. This bitter

taste was caused by saponin compounds.[11] This compound could lower blood glucose levels[12] and had activity as antihypertensive to lower blood pressure.[13]

Papaya leaves could be processed into various foods, one of them was jelly. It had been proven by a preliminary study of papaya leaves jelly and had a good acceptance response. Food innovation was done to reduce bitterness and improve taste with addition other foodstuffs. The composition of this product was papaya leaves juice, jelly, stevia powder and skim milk. Each of the ingredients in this product had a positive effect for people with diabetes who have high blood pressure.

The agar-agar fibers act as anti-hyperglycemic because they increasing insulin sensitivity,[14] and lowering blood pressure through increased endothelial function.[15] Stevia had anti-hyperglycemy [16] and antihypertensive effects lowering blood pressure by increasing vasodilation of blood vessels.[17] Skim milk may trigger insulin secretion and slow the absorption of nutrients so that glucose levels will be controlled and hyperglycemia did not occur.[18] In addition, skim milk could also help the body in regulating endothelial function associated with the elasticity of blood vessels.[19]

Some studies have shown that chlorophyll could lower blood glucose and lipid profile. Otherwise, research on the effects of chlorophyll on blood pressure was very limited. However, the relationship between blood glucose and lipid profile to blood pressure was very close.

METHODS

This research was included in clinical nutrition scope conducted in Semarang city which covers residential area and office. Data collected from the screening process of research subjects was conducted from March to June 2016. The design study used a true experiment design with pre-test post-test control group design.

Total subjects were calculated using unpaired numerical analytic formulas with standard deviations 12.88 based on previous study.[20] The results of the calculations were augmented 10% to anticipate the drop-out and found 10 people per group. The total subjects used in this study were 27 people, 14 people including the control group and 13 people including the treatment group. The control group was given a papaya leaves jelly while the control group was given a jelly with a green dye.

Subjects were obtained through two screening stages. The first stage through the criteria Body Mass Index (BMI) ≥ 23 kg / m^2, women aged 35-50 years, waist circumference > 80 cm, not consuming alcohol, not smoking, not taking anti-hiperglichemy and anti-hypertensive drugs, not being pregnant or breastfeeding. Second stage screening was having Fasting Blood Sugar (FBS)> 90 mg/dl, willing to comply with research procedures and signing informed consent (IC).

The dependent variable in this research was papaya leaves jelly. The independent variables used were systolic and diastolic blood pressure. Confounding variables used were intake of fiber, sodium, potassium, calcium, magnesium, and physical activity.

The data of food intake was obtained using recall form in 3 times (2 times on weekday and 1 day at weekend) while physical activity data using International Physical Activity (IPAQ) form that obtained in 3 times data retrieval. Blood pressure data were taken before and after the intervention. Blood pressure was measured using digital sphygmomanometer. Anthropometric data of body weight was measured using a digital weight scales with 0.1 kg precision and height measured using microtoise with 1 mm accuracy. Compliance data was obtained from filling out the checklist form filled by the researcher through direct observation while the subject consuming the product.

The safe dose to lower blood pressure were based on dose that used Panam Parikh study to lower blood glucose and lipid profile.[21] The Parikh Precious study gave daily spirulina supplementation of 8 grams that containing 60,8 mg of chlorophyll for 60 days. Based on laboratory test, 8,1 gram papaya leaves jelly of contains 7,4% chlorophyll. The dose given to the respondents was 24,6 grams of papaya leaves jelly containing 182,4 mg of chlorophyll for 20 days.

Normality test using Saphiro-Wilk because the subject used less than 50 subjects. The relationship between two variables could be seen from the results of bivariate analysis. Differences in systolic blood pressure (SBP) before and after intervention were analyzed using paired t-test while diastolic blood pressure (DBP) differences before and after intervention were analyzed using Wilcoxon. The difference of SBP in the treatment group and the control group was analyzed using independent t-test while the difference of DBP in the treatment group and control group was analyzed using Mann Whitney. ANCOVA test was performed to see the effect of papaya leaves jelly after controlled by confounding variables.

RESULTS

Characteristics of the subject

Subjects that fulfill inclusion criteria were 27 people which obtained from screening at Sendangmulyo and Tandang (Tembalang Sub-district) and Semarang City Government office in Pandanaran Building. Total subjects who screened were 221 person, 27 subjects were selected, 13 subjects were in the treatment group and 14 subjects were in the control group.

The comparison of characteristics before intervention between the treatment group and the control group showed in table 1. Statistical analysis shows that the characteristics between the treatment group and the control group was no different (p> 0.05).

Data on Nutrient Intake and Physical Activity

Based on table 1, it could be concluded that there was no difference in average intake of fiber, potassium, calcium, magnesium, and physical activity in both groups (p> 0.05) but there was a significant difference in sodium intake where the percent of sodium sufficiency in the treatment group was higher than the control group.

Blood Pressure Difference Before and After Intervention

Table 2 shows that there was a difference between systolic and diastolic blood pressure before and after intervention in the treatment group (p <0.05). However, there was no difference in the control group for both systolic and diastolic blood pressure before and after intervention (p> 0.05).

Differences in Blood Pressure between Treatment Group and Control Group

Table 3 shows that there was no difference change in systolic or diastolic blood pressure or decrease in the treatment and control group (p> 0.05).

Table 1. Characteristics of subjects before intervention and data of nutritional adequacy and physical activity during treatment

Characteristic/ Variable	Treatment (n=13)	Control (n=14)	p-value
	mean±SD	mean±SD	
Age (years)	43.46±4.29	43.57±3.39	0.94[a]
FBS (g/dl)	101.62±10.04	97.93±9.31	0.33[a]
BMI (kg/m^2)	28.10±3.18	28.98±2.70	0.44[a]
Waist circumference (cm)	89.43±5.53	88.83±7.29	0.54[b]
SBP pre (mmHg)	131.15±25.98	124.21±19.80	0.31[b]
DBP post (mmHg)	90.54±12.70	86.86±16.02	0.18[b]
Fiber intake (%)	25.40±14.31	26.82±20.88	0.88[b]
Natrium intake (%)	24.35±20.27	14.07±17.34	0.05[b*]
Kalium intake (%)	23.76±8.15	18.62±7.14	0.09[a]
Kalsium intake (%)	23.61±12.85	17.52±8.67	0.17[b]
Magnesium intake (%)	49.60±12.83	52.92±25.92	0.92[b]
Physical activity (MET-minute)	3822.40±2051.96	4193.0±5241.23	0.38[b]

[a] Independent t-test
[b] Mann-Whitney test
*significantly different

Table 2. Blood Pressure Blood Test Results Before and After Intervention

Variable	Treatment (n=13)			Control (n=14)		
	Before (mean±SD)	After (mean±SD)	p-value	Before (mean±SD)	After (mean±SD)	p-value
SBP (mmHg)	131.15±25.98	124.92±26.41	0.01[a*]	124.21±19.80	119.86±16.08	0.12[a]
DBP (mmHg)	90.54±12.70	85.54±14.09	0.01[b*]	86.86±16.02	84.07±10.23	0.47[b]

[a] *Paired t test*
[b] *Wilcoxon*
**signifikan*

Table 3. Differential Test Results of Blood Pressure Changes Between Treatment Group and Control Group

Variable	Treatment (Mean±SD)	Control (Mean±SD)	Sig p
ΔSBP (mmHg)	-6.23±7,21	-2.21±14.26	0.37[a]
ΔTDP (mmHg)	-5.00±7,90	-4.93±14.85	0.63[b]

[a] *Independent t test*
[b] *Mann-Whitney*

MAKING OF PAPAYA LEAVES JELLY (3 serving, 9 grams per serve)

1. Tools and Materials

a. Tools
   1) Pans
   2) Blender
   3) Strainer
   4) Basin
   5) Mold jelly

b. Materials
   1) 50 gr papaya leaves
   2) 30 gr "ampo"
   3) 50 ml low fat milk
   4) 2 gr stevia sugar
   5) 0.5 gr jelly powder
   6) Water

2. Procedure

Prepare the papaya leaves by washing and remove any dirt. Boil the papaya leaves jelly and "ampo" with water. Wash papaya leaves with running water until theres is no "ampo" left in the leaves. Blend papaya leaves with skim milk then strain the juice. Cook the juice with jelly powder and stevia sugar in pan while stirring until boiling. Pour the jelly into the mold.

DISCUSSION

Characteristics subjects by age, FBS, BMI, waist circumference, pre SBP and pre DBP between treatment group and control group had p> 0.05. This suggests that the characteristics of the subject between the group and the treatment were same. This test should be performed before the intervention so that the initial characteristics of the subject between the two groups were equal. Homogeneity of preliminary data was required for experimental research so not confounding the final data of the study.

There was no difference in nutritional intake and physical activity of the subjects between treatment and the control group during intervention except sodium intake. Sodium intake in the treatment group was higher than in the control group. Several subjects in the treatment group ate high-sodium foods such as salted fish, instant noodles, light snacks with flavorings and artificial preservatives. Nutrition education had been conducted on balanced nutrition in both groups as an effort to control intake. This was done so the subject of eating foods as needed.

Based on the dependent difference test using paired t test and wilcoxon, there was a significant decrease in systolic and diastolic blood pressure after intervention in the treatment group but there was no significant reduction in systolic and diastolic blood pressure in control group. Decreasing systolic and diastolic blood pressure in the treatment group caused by papaya leaves content in jelly. The state of hypertension was closely related to oxidative stress in the body. Oxidative stress that may occur due to hyperglycemia in this prediabetic woman could result in the function and decreasing Nitric Oxide (NO) amount.[22] NO was a compound could maintain the elasticity of blood vessels. Decreasing NO will cause its function as a vasodilator was not optimal and will increase blood pressure. In addition, the state of oxidative stress also resulted in reduced antioxidant compounds that used as a neutralizer of prooxidant compounds.

Papaya leaves contain several antioxidant compounds that could balance the state of oxidative stress. There were several possible mechanisms for blood pressure reduction: 1) Chlorophyll in papaya leaves could give additional electrons to free radicals 2) chloroplasts also contain superodide dismutase (SOD) compounds that could catalyze superoxide radicals (O_2) 3) Saponin in papaya leaves could combine superoxide radicals.[23]

Beside containing antioxidant compounds, papaya leaves also have compounds that have a positive effect on blood pressure. Magnesium contained in papaya leaves had a function to regulate the pressure and reactivity of blood vessels by altering the response of vasoconstrictors and vasodilatators. Increased magnesium concentration could cause vasodilation, improve blood flow, decrease vascular resistance, and increase arterial function. In vascular smooth muscle cells, magnesium inhibits calcium into cells and acts as an antagonist of calcium that triggers

vasoconstrictive activity.[8] Studies conducted by Gurrero Romero showed decreasing systolic and diastolic blood pressure after taking magnesium supplementation.[8] Saponin compounds, could also lower blood pressure by preventing RAAS (Renin Angiotensin Aldosteron System) by inhibiting the production of renin which was a component of RAAS.[13]

There was no difference in systolic and diastolic blood pressure changes between treatment and control group. This case happened because the jelly products that were administered in both groups equally contain fiber, skim milk and stevia sweeteners that also have the effect to lower blood pressure. The fibers contained in jelly could lower blood pressure by improving blood vessel endothelial function and increase mineral absorption that indirectly affects blood pressure such as magnesium and potassium.[24] Skim milk contains calcium, magnesium and potassium minerals that have a positive effect on blood pressure. In addition to minerals, digested milk proteins will produce peptides that could inhibit angiotensin-1-converting enzymes that will regulate endothelial function.[19] Stevia sweeteners used in jelly-making also have antihypertensive effects by triggering vasodilation and diuresis (including natriuresis) volume of plasma so that blood pressure drops.[17]

Decreasing SBP and DBP in treatment group showed a synergistic effect of the compound on papaya leaves with other foodstuff. Therse no difference changes between SBP and DBP in both groups because the dose of papaya leaves was less so the effect was less noticeable too. It was need to research about the addition of papaya leaves dose to see the effect of papaya leaves against the decrease in blood pressure. Research conducted by Nissa et al showed there were two variations of chlorophyll dose and higher doses had greater antioxidant activity as well.[23] The limited research showing the effect of chlorophyll on blood pressure could be basic of subsequent research. In addition, it was also necessary to do similar research with longer duration of time. Research of Panam Parikh by using chlorine-rich spirulina performed for 60 days showed significant results on the decrease of blood glucose.[21] Normal blood glucose could prevent oxidative stress to prevent the occurrence of hypertension.[25]

There was a significant decrease in systolic and diastolic blood pressure in the treatment group but not in control group. The test showed that there was no effect of confounding variables on the decrease of SBP and DBP in treatment group.

Test the content of nutrients and non-nutrients needs to be done to find out what and how much the content of papaya leaves jelly. Need further research with varying doses in order to know the effect of papaya leaves jelly to blood pressure. Furthermore, duration of giving papaya leaves jelly could also be enhanced to determine the effectiveness of papaya leaves jelly in lowering blood pressure.

REFERENCES

1. **Association AD**. Diagnosis and Classification of Diabetes Mellitus. 2013;36:67–74.
2. **Defronzo RA, Abdul-ghani M.** Assessment and Treatment of Cardiovascular Risk in Prediabetes : Impaired Glucose Tolerance and Impaired Fasting Glucose. AJC [Internet]. Elsevier; 2011;108(3):3B – 24B. Available from: http://dx.doi.org/10.1016/j.amjcard.2011.03.013
3. **Xu,** Detection Of Rediabetes And Undiagnosis Tye 2 Diabetes: A Large Oulation Based Study.
4. **Satevo J, Kautainen H.** Gender Differences In Adiponect And Low- Grade Inflamation Among Individuals With Normal Glucose Tolerance, Prediabetes, And Type 2 Diabetes. 2009
5. **Stas SN, El-atat FA, Sowers JR**. Pathogenesis of Hypertension in Diabetes. 2004;221–5.
6. **EFSA**. Scientific Opinion on the substantiation of health claims related to superoxide dismutase (SOD) and protection of DNA , proteins and lipids protection of the skin from photo-oxidative (UV-induced) damage (ID 2305 , 3161), reduction of muscle fatigue. 2010;8(1924):1–20.
7. **Marquez dkk**. Antioksidant activity of chlorophylls and their derivates. Food Research International.2005;38:885-891.
8. **Guerrero-Romero MR´-M´**. The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels : a randomized , double- blind , placebo-controlled clinical trial. 2008;1–7.
9. **Barbagallo M, Dominguez LJ**. Diabetes and Clinical Research Magnesium and Type 2 Diabetes : An Update ClinMed. 2015;1–5.
10. **Setiari N**. Eksplorasi Kandungan Klorofil pada beberapa Sayuran Hijau sebagai Alternatif Bahan Dasar Makanan Tambahan. 2009;11(1).

11. **Ayoola PB**, Adeyeye a. Phytochemical and Nutrient Evaluation of Carica Pepaya (Pawpaw) Leaves. Ijrras. 2010;5(3):325–8.
12. **Zheng T, Shu G, Yang Z, Mo S, Zhao Y, Mei Z**. Antidiabetic effect of total saponins from Entada phaseoloides (L .) Merr . in type 2 diabetic rats. J Ethnopharmacol [Internet]. Elsevier Ireland Ltd; 2012;139(3):814-21. Available from: http://dx.doi.org/10.1016/j.jep.2011.12.025
13. **Chen M, Long Z, Wang Y, Liu J, Pian HAI, Wang L, et al**. Protective effects of saponin on a hypertension target organ in spontaneously hypertensive rats. 2013;429–32.
14. **Weickert MO, Pfeiffer AFH**. Metabolic Effects of Dietary Fiber Consumption and Prevention of Diabetes 1. 2008;(October 2007):439–42.
15. **Geleijnse JM**. Dietary Fiber and Blood Pressure. 2006;165:150–6.
16. **Jeppesen PB, Gregersen S, Rolfsen SED, Jepsen M, Colombo M, Agger A, et al**. Antihyperglycemic and Blood Pressure-Reducing Effects of Stevioside in the. 2003;52(3):372–8.
17. **Chatsudthipong V, Muanprasat** C. Pharmacology & Therapeutics Stevioside and related compounds : Therapeutic bene fi ts beyond sweetness. Pharmacol Ther [Internet]. Elsevier Inc.; 2009;121(1):41–54. Available from: http://dx.doi.org/10.1016/j.pharmthera.2008.09.007.
18. **Margolis KL, Wei F, Boer IH De, Howard B V, Liu S, Manson JE, et al**. A Diet High in Low-Fat Dairy Products Lowers Diabetes Risk in Postmenopausal Women 1 , 2. 2011;
19. **Elwood PC, Pickering JE, Givens DI, Gallacher JE**. The Consumption of Milk and Dairy Foods and the Incidence of Vascular Disease and Diabetes : An Overview of the Evidence. 2010;925–39.
20. **Lee S, Park HK, Son SP, Lee CW, Kim IJ, Kim HJ**. Effects of oral magnesium supplementation on insulin sensitivity and blood pressure in normo- magnesemic nondiabetic overweight Korean adults. Nutr Metab Cardiovasc Dis [Internet]. Elsevier Ltd; 2009;19(11):781–8. Available from: http://dx.doi.org/10.1016/j.numecd.2009.01.002
21. **Panam Parikh, Uliyar Mani UI**. Role of Sopirulina in the Control of Glycemia and Lipidemia in Type 2 Diabetes Mellitus. 2001. p. 193–9.
22. **Grossman E.** Does Increased Oxidative Stress Cause Hypertension?. Diabetes Care. 2008;31:185-189.
23. **Nissa C, Kartasurya MI, Rahmawati B**. Effects of Chlorophyll in Papaya Leaves on Superoxide Dismutation and Blood Glucose Level of Diabetic Rats. Makara J Heal Res [Internet]. 2015;19(2):75–80. Available from: http://journal.ui.ac.id/index.php/health/article/view/5179
24. Jarz K, Machnik G, Adamczyk J, Belowski D, Obuchowicz E, Urbanek T. Superoxide dismutase 1 and glutathione peroxidase 1 are involved in the protective effect of sulodexide on vascular endothelial cells exposed to oxygen – glucose deprivation. 201

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