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The Effect of Steeping Water Temperature Of Cinnamon *(Cinnamomum Burmannii)* and Steeping Time With Test Time on the Glycemic Response of Diabetic Rats

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ABSTRACT

Diabetes Mellitus (DM) is a disease in which the body is unable to metabolize fats, proteins and carbohydrates which is characterized by high blood glucose levels or commonly known as hyperglycemia. Until 2019, 10.9 million DM cases were found in Indonesia and are suspected of continuing to increase. Cinnamon (Cinnamomum Burmannii) has several active ingredients vizcoumarin, cinnamat, cinnamaldehid, polyphenols and flavonoid can increase glucose transport by GLUT 4 in adipose cells and skeletal muscles so as to significantly reduce blood glucose. Thus, cinnamon has the potential to be a useful product for the community, namely a diabetes herbal medicine. The purpose of this research was to determine the ratio of the temperature of the cinnamon steeping water with the duration of steeping on the glycemic response of diabetic rats.

This research uses Completely randomized design (CRD) with 2 factors, namely the first factor (P): steeping water temperature (65 °C, 75 °C, and 85 °C) and brewing time (20 minutes, 25 minutes and 30 minutes) and the second factor (L): test time (30 minutes, 60 minutes, 90 minutes and 120 minutes). This study also carried out control (-) and control (+) as a preliminary study to determine the glycemic response in test animals. Each treatment will be repeated 3 times to obtain 33 experimental units. The parameters analyzed were blood sugar levels, the percentage (%) increase in blood sugar levels, and the percentage (%) decrease in blood sugar levels.

The results showed that temperature of the cinnamon steeping water (Cinnamomum Burmannii) and the duration of brewing can reduce the blood sugar levels of mice every time the test is carried out. The best treatment was obtained from the ratio of the temperature of the steeping water and the duration of steeping, namely 65 °C and brewing time for 25 minutes, determined based on the percentage decrease in blood sugar level, which is equal to 53,02%.

Keywords: Cinnamon, antidiabetic activity, temperature and brewing time, herbal drink

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INTRODUCTION:

Diabetes mellitus (DM) is a disease in which the body is unable to metabolize fats, proteins and carbohydrates which is characterized by high blood sugar or commonly called [1]. According to the World Health Organization (WHO), in 2017, 425 million patients worldwide suffered from diabetes mellitus. It is estimated that this figure will increase by 45% or the equivalent of 629 million patients with diabetes mellitus in 2045. Indonesia ranks 6th out of ten countries with the highest number of people suffering from diabetes mellitus, in 2017, the number of patients is 10.3 million and this is estimated to increase to 16.7 million patients in 2045 [2]. DM disease can be controlled with proper management to prevent complications. Management of DM includes pharmacological and non-pharmacological management.

Long-term pharmacological treatment, the use of anti-glycemic drug preparations has many side effects, so it is necessary to have more effective and safer preparations such as herbal medicines derived from plants, including the one is cinnamon powder [3]. Cinnamon contains cinamaldehid, eugenol, cinnamic acid, catechins, epicatechins and other polyphenolic compounds.Some studies say that*cinnamaldehid* can increase glucose transport by GLUT 4 into fat cells and skeletal muscle to significantly lower blood sugar [4].Cinnamon has a sweet, fragrant aroma, is warm, has a spicy, but slightly sweet taste. The euganol and polyphenol content in cinnamon may help increase insulin receptor proteins in cells, thereby increasing insulin sensitivity and reducing glucose levels to near normal levels. This is supported by a research conducted by Darfiani (2015) who conducted a research by giving 7 grams of cinnamon tea for 3 days to 20 respondents. The results of the study are that there is a significant effect of giving cinnamon powder which can reduce blood sugar levels in patients with diabetes mellitus [5].

MATERIALS AND METHODS

The materials used in this study were cinnamon (*Cinnamon from Zeylan*) obtained from the city of Medan. Male test animals*mus musculus blanc*2-3 month old mice with a body weight of 20-30 grams,mice are fed in the form of CP 521 pellets (with a composition of 10% protein, 3% fat, 8% fiber and 12% moisture). The chemicals used are Alloxane monohydrate, Ethanol 96%,*Aquabidestilasi sterile for injection*, and metformin. The tools used in this study were animal scales (*triple beam*scale), electric scale (precisa), cage, set of infundation extraction tools, oral syringes, 1ml syringes, glucostest, micropipettes (socorex), scalpel, rotary evaporator (stuart), rat racks and tools glass (pyrex).

RESEARCH DESIGN

This study used a 2-factor completely randomized factorial (CRD) design. The first factor is the steeping water temperature and steeping time, the second factor is the test time. Each treatment will be repeated 3 times to obtain 27 experimental units (Table 1). This study was also performed with control (-) and control (+) as a preliminary study to determine the glycemic response in test animals.

Control (-) = alloxan + Cinnamon powder without soaking

Control (+) = Alloxan + Metformin

Table 1: Research design

Cinnamon steeping water temperature and steeping time	Testing Time			
	L_1 (30 minutes)	L_2 (60 minutes)	L_3 (90 minutes)	L_4(120 minutes)
P_1 (65 ^{O}C and 20 minutes)	$\mathbf{P_1L_1}$	$\mathbf{P_1L_2}$	$\mathbf{P_1L_3}$	$\mathbf{P_1L_4}$
P_2 (65 ^{O}C and 25 minutes)	$\mathbf{P_2L_1}$	$\mathbf{P_2L_2}$	$\mathbf{P_2L_3}$	$\mathbf{P_2L_4}$
P_3 (65 ^{O}C and 30 minutes)	$\mathbf{P_3L_1}$	$\mathbf{P_3L_2}$	$\mathbf{P_3L_3}$	$\mathbf{P_3L_4}$
P_4 (75 ^{O}C and 20 minutes)	$\mathbf{P_4L_1}$	$\mathbf{P_4L_2}$	$\mathbf{P_4L_3}$	$\mathbf{P_4L_4}$
P_5 (75 ^{O}C and 25 minutes)	$\mathbf{P_5L_1}$	$\mathbf{P_5L_2}$	$\mathbf{P_5L_3}$	$\mathbf{P_5L_4}$
P_6 (75 ^{O}C and 30 minutes)	$\mathbf{P_6L_1}$	$\mathbf{P_6L_2}$	$\mathbf{P_6L_3}$	$\mathbf{P_6L_4}$
P_7 (85 ^{O}C and 20 minutes)	$\mathbf{P_7L_1}$	$\mathbf{P_7L_2}$	$\mathbf{P_7L_3}$	$\mathbf{P_7L_4}$
P_8 (85 ^{O}C and 25 minutes)	$\mathbf{P_8L_1}$	$\mathbf{P_8L_2}$	$\mathbf{P_8L_3}$	$\mathbf{P_8L_4}$
P_9 (85 ^{O}C and 30 minutes)	$\mathbf{P_9L_1}$	$\mathbf{P_9L_2}$	$\mathbf{P_9L_3}$	$\mathbf{P_9L_4}$

Test *and instantly* antidiabetic activity

Mice were fed CP 521 pellets (with a composition of 10% protein, 3% fat, 8% fiber and 12% water) followed by infused cinnamon powder and then performed antidiabetic tests on mice that had been induced diabetes with water powder soaking Cinnamon *(Cinnamomum zeylanicum)*.

Testing for antidiabetic activity in laboratory animals*and instantly*, Test the antidiabetic effect according to the method described by Susilawati,*et al.*(2019), test animals were divided into five groups, namely: 1) Negative control (no treatment), (2) Metformin 45 mg/kg BW as positive control, (3) Cinnamon (*Cinnamomum zeylanicum*) temperature 65 ºC infusion time 20 minutes, 25 minutes and 30 minutes (4) Cinnamon (*Cinnamomum zeylanicum*) temperature 75 ºC infusion time 20 minutes, 25 minutes and 30 minutes (5) Cinnamon (*Cinnamomum zeylanicum*) temperature 85 ºC infusion time 20 minutes, 25 minutes, 30 minutes, administered orally. Then each group was induced with alloxan intraperitoneally. On day 13, a blood sample was taken (initial). Then each group received its own treatment. Then, after 30 minutes, 60 minutes, 90 minutes and 120 minutes, blood glucose levels were measured.

Data analysis

1. Calculation of percentage (%) increase in test group's blood sugar:

$$\% = \frac{(P-Q)}{Q} x100\%$$

P = Blood sugar level after alloxan induction
Q = baseline blood sugar level

2. Calculation (%) of test group blood glucose decrease:

$$\% = \frac{(P-Q)}{P} x100\%$$

P = Blood sugar level after alloxan induction
Q = Blood sugar level 14 days after treatment

RESULTS AND DISCUSSION

Percent Effect of Alloxan Induction on Raising Blood Glucose in Mouse Laboratory Animals

Table 2: Mean Value of Percentage (%) Increase in Blood Glucose in Mice After Alloxan Induction

Test group (F)	Blood sugar level (mg/dl)		Percentage increase (%)
	Early	Alloxan	
Negative control	107,00 ± 2,65	174,33 ± 5,03	63,00 ± 6,48
Positive control	106,67 ± 2,08	181,67 ± 10,02	70,25 ± 6,49
Temperature 65 °C 20 minutes	97,33 ± 2,52	491,33 ± 29,30	405,52 ± 42,53
Temperature 65 °C 25 minutes	106,00 ± 4,58	444,00 ± 75,72	317,95 ± 62,00
Temperature 65 °C 30 minutes	104,33 ± 6,03	328,00 ± 21,00	214,61 ± 17,14
Temperature 75 °C 20 minutes	104,67 ± 1,53	292,00 ± 8,19	179,10 ± 11,95
Temperature 75 °C 25 minutes	104,67 ± 7,57	228,00 ± 25,51	117,95 ± 19,89
Temperature 75 °C 30 minutes	105,67 ± 6,81	201,33 ± 4,16	91,24 ± 16,50
Temperature 85 °C 20 minutes	107,00 ± 3,61	192,00 ± 2,65	79,62 ± 8,30
Temperature 85 °C 25 minutes	109,33 ± 2,52	185,00 ± 5,29	69,20 ± 2,17
Temperature 85 °C 30 minutes	102,67 ± 4,04	176,00 ± 2,00	71,65 ± 8,63

Notes: The test was carried out 4 times, the sign (±) indicates the value of the standard deviation

Mice which will be used beforehand in the alloxan induction at a dose of 150 mg/KgBB. This induction is useful in increasing levels of diabetes in mice so that they can be categorized as hyperglycemic mice. Mice are expressed in a diabetic state when mean blood glucose ≥ 140 mg/dl [6].

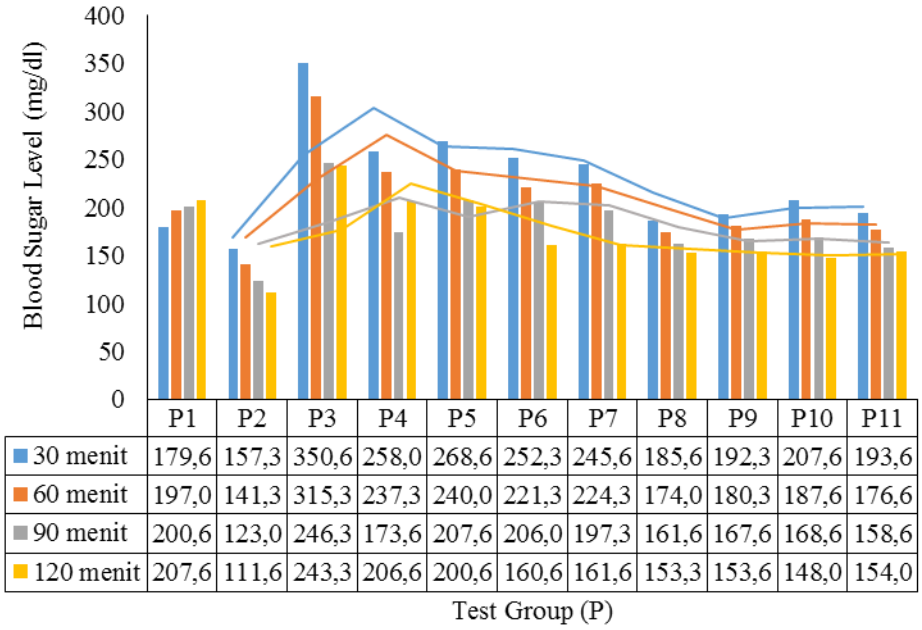
The Effect of Cinnamon Steep Water Temperature and Infusion Time on The Glycemic Response of Diabetic Mice

The blood sugar levels of the mice during the test i.e. 30, 60, 90 and 120 minutes can be seen in Table 3 and Figure 1. The percentage (%) decrease in response glycemia of diabetic mice can be seen in Table 4.

Table 3: Blood sugar levels (mg/dl) in mice during testing

Test group (F)	Blood sugar level (mg/dl)			
	30 minutes	60 minutes	90 minutes	120 minutes
Negative control	179,67 ± 4,73	197,00 ± 7,00	200,67 ± 6,43	207,67 ± 6,43
Positive control	157,33 ± 6,03	141,33 ± 3,06	123,00 ± 15,13	111,67 ± 10,41
Temperature 65 °C 20 minutes	350,67 ± 158,99	315,33 ± 128,25	246,33 ± 123,43	243,33 ± 104,75
Temperature 65 °C 25 minutes	258,00 ± 109,99	237,33 ± 107,97	173,67 ± 23,76	206,67 ± 72,14
Temperature 65 °C 30 minutes	268,67 ± 78,55	240,00 ± 63,51	207,67 ± 58,14	200,67 ± 36,94
Temperature 75 °C 20 minutes	252,33 ± 26,95	221,33 ± 33,47	206,00 ± 34,60	160,67 ± 20,43
Temperature 75 °C 25 minutes	245,67 ± 41,65	224,33 ± 24,19	197,33 ± 22,19	161,67 ± 14,15
Temperature 75 °C 30 minutes	185,67 ± 7,64	174,00 ± 7,81	161,67 ± 9,71	153,33 ± 13,32
Temperature 85 °C 20 minutes	192,33 ± 17,50	180,33 ± 14,57	167,67 ± 15,37	153,67 ± 2,08
Temperature 85 °C 25 minutes	207,67 ± 23,59	187,67 ± 13,50	168,67 ± 5,03	148,00 ± 11,27
Temperature 85 °C 30 minutes	193,67 ± 8,08	176,67 ± 9,87	158,67 ± 3,21	154,00 ± 5,20

Notes: The test was carried out 4 times, the sign (±) indicates the value of the standard deviation



	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11
30 menit	179,6	157,3	350,6	258,0	268,6	252,3	245,6	185,6	192,3	207,6	193,6
60 menit	197,0	141,3	315,3	237,3	240,0	221,3	224,3	174,0	180,3	187,6	176,6
90 menit	200,6	123,0	246,3	173,6	207,6	206,0	197,3	161,6	167,6	168,6	158,6
120 menit	207,6	111,6	243,3	206,6	200,6	160,6	161,6	153,3	153,6	148,0	154,0

Information:

P_1 = Control (-)
P_2 = Control (+)
P_3 = Temperature 65 ^{O}C 20 minutes
P_4 = Temperature 65 ^{O}C 25 minutes
P_5 = Temperature 65 ^{O}C 30 minutes
P_6 = Temperature 75 ^{O}C 20 minutes
P_7 = Temperature 75 ^{O}C 25 minutes
P_8 = Temperature 75 ^{O}C 30 minutes
P_9 = Temperature 85 ^{O}C 20 minutes
P_{ten} = Temperature 85 ^{O}C 25 minutes
P_{11} = Temperature 85 ^{O}C 30 minutes

Figure 1: Blood sugar levels in mice

Based on Table 3 and Figure 1 above, it can be seen that the glycemic response in diabetic mice at 30 minutes is still low, but the longer the test time, i.e. up to 'at the 120th minute, the glycemic response of diabetic mice increases.

Different blood glucose levels in each treatment illustrate the effect of test time at 20, 30, 60, 90, and 120 minutes on the glycemic response of mice (Table 3). In the graph of glycemic response in control and all treatments, cinnamon dip water temperature and infusion duration elicited a response by reducing blood glucose levels in mice diabetics.

The peak of the glycemic response also occurs at the same time after 30 minutes of administration and there is a fairly rapid decrease after 60 minutes of administration until after 120 minutes of administration. This could be because cinnamon powder contains quite high bioactive compounds in the form of antioxidant compounds [7] which play a role in inhibiting glucose uptake into the blood. This research is consistent with research by Bernardo et al. (2015) who used cinnamon tea and contains pilophenol in the tea which acts as an antioxidant. Polyphenolic compounds play an important role in insulin secretion in pancreatic beta cells [8]. Research by Syahfitri et al (2023) indicates that cinnamon extract has a very high antioxidant activity value i.e. 30.26 ppm or <50 ppm [9].

The results of this study are in line with previous studies which indicated that the peak in blood glucose content occurs after 30 minutes of administration, after the 30th minute it tended to decrease significantly [10]. Therefore, cinnamon infusion water has the potential to be used as a functional drink for humans with high blood sugar or diabetes. For the people of Indonesia, as described by [11], traditional medicine plays an important role in maintaining health and will continue amid the development of modern medicine.

Table 9 also shows that in each treatment group there was an increase in the percentage decrease in blood glucose, but in group 1 there was no percentage decrease, this is because the group 1 received no treatment after alloxan induction. The difference in percent reduction for each group was different, this was due to a relationship between the temperature of the soaking water and the infusion time of the cinnamon given to the diabetic mice.

Table 4: Percent decrease in glycemic response (%) diabetic mice

Test group (K)	Percent decrease in glycemic response (%)			
	30 minutes	60 minutes	90 minutes	120 minutes
Negative control	-3,10 ± 3,26	-13,04 ± 4,08	-15,24 ± 7,03	-19,25 ± 6,94
Positive control (metformin)	13,11 ± 7,89	22,05 ± 4,61	32,18 ± 9,11	38,42 ± 6,62
Temperature 65 ^{o}C 20 minutes	28,56 ± 31,36	35,68 ± 25,64	50,30 ± 22,91	51,15 ± 18,79
Temperature 65 ^{o}C 25 minutes	41,99 ± 20,72	46,76 ± 20,31	60,38 ± 6,09	53,02 ± 14,72
Temperature 65 ^{o}C 30 minutes	17,22 ± 28,50	26,20 ± 22,89	36,07 ± 21,08	38,61 ± 12,04
Temperature 75 ^{o}C 20 minutes	13,70 ± 7,11	24,34 ± 9,56	29,63 ± 9,77	44,87 ± 8,16
Temperature 75 ^{o}C 25 minutes	-8,05 ± 17,77	1,20 ± 11,18	13,33 ± 5,84	28,96 ± 2,00
Temperature 75 ^{o}C 30 minutes	7,73 ± 5,09	13,53 ± 4,76	19,62 ± 6,22	23,82 ± 6,80
Temperature 85 ^{o}C 20 minutes	-0,25 ± 10,28	6,03 ± 8,39	12,64 ± 8,35	19,95 ± 2,15
Temperature 85 ^{o}C 25 minutes	-12,11 ± 10,42	-1,39 ± 5,40	8,83 ± 1,18	19,84 ± 8,48
Temperature 85 ^{o}C 30 minutes	-10,07 ± 5,42	-0,38 ± 5,60	9,83 ± 2,80	12,49 ± 3,10

Notes: The test was carried out 4 times, the sign (±) indicates the value of the standard deviation,

The mice that received metformin were also effective in reducing blood sugar levels, i.e. the percentage reduction was 38.42%. This is because metformin works by helping to restore the body's response to the insulin normally produced by the body. This medicine will subsequently reduce the excess sugar produced during the day and also absorbed by the intestines. The usual dose of metformin consumed by adults is 500 mg orally once a day or depending on the severity of the disease and the condition of the patient. However, for children there are no dosage provisions, as this medicine can be dangerous for children. Side effects after consuming metformin are nausea, vomiting, diarrhea, fatigue and weakness, and stomach ulcers. Therefore, many people nowadays turn to herbal medicines which will be consumed and do not have as many side effects as chemical diabetes medicines [12].

Test group P_4 (boiling water temperature 65 ^{o}C which was infused for 25 minutes) was the test group with the highest percentage reduction in blood sugar levels, namely 53.02%, as according to [13] this was because that a number of bioactive compounds were suspected to have antidiabetic properties the activity of cinnamon, as described in the study [14] indicates that cinnamaldehyde has biological activity as an antioxidant , antiviral, antifungal and antibacterial. Thus, cinnamaldehyde significantly lowers blood sugar levels, increases sensitivity and improves insulin. Many people use it to lower blood sugar in people with diabetes mellitus.

Test group P_{11} (soaking water temperature 85 ^{o}C which is infused for 30 minutes) is the lowest percentage reduction in blood sugar level, which is equal to 12.49%. Indeed, antioxidants are oxidized by heating temperatures. According to (Aikkarach et al., 2018) [15], heating can accelerate the oxidation of antioxidants contained in a material. Heating to high temperatures can damage heat-resistant components, including phenolics. The steeping process is 85 ^{o}C that was steeped for 30 minutes reduced the antioxidant activity of cinnamon.

The main flavonoids in cinnamon sticks are quercitrin and fluoretin which also function as antioxidants. In people with DM, there is an increase in the number of free radicals because they are produced in the body in an imbalanced state. Flavonoids have an antioxidant effect which acts as an antidote to free radicals such as reactive oxygen species (ROS) [16]. Flavonoids act by inhibiting glucose reabsorption by the kidneys [17], regulating the action of enzymes involved in carbohydrate metabolism pathways, increasing insulin secretion [18].

According to Chougale et al. (2007), the administration of alloxan at a dose of 140 mg/kg body weight would increase blood glucose levels in rats on the 5th day after induction. Thus, in this study, administration of a dose of 150 mg/kg body weight showed that alloxan- induced mice diabetic [19].

Alloxan's mechanism of action can partially damage the pancreas so that the pancreas can still produce insulin. Alloxa selectively inhibits glucose-induced insulin secretion through inhibition of specific glucokinase, a glucose sensor on beta cells that can lead to insulin-dependent diabetes through its ability to induce the formation of reactive species of oxygen (ROS), resulting in selective beta cell necrosis (Lenzen, 2008) [20]. Test animals with diabetes were prepared to be treated with the following groups: 1) Negative control (no treatment), (2) Metformin 45 mg/kgBB as positive control, (3) Cinnamon (*Cinnamomum Burmannii*) temperature 65 ºC infusion time 20 minutes, 25 minutes and 30 minutes (4) Cinnamon (*Cinnamomum Burmannii*) temperature 75 ºC infusion time 20 minutes, 25 minutes and 30 minutes (5) Cinnamon (*Cinnamomum Burmannii*) temperature 85 ºC infusion time 20 minutes, 25 minutes, 30 minutes.

CONCLUSION

The cinnamon steep water gave different responses with each treatment, the best infusion was from the cinnamon stick powder with a temperature ratio of 65 ^{o}C and the infusion time is 25 minutes, determined by the percentage reduction in blood sugar, which is 53.02%.

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