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Activity Test of Cinnamon Extract (*Cinnamomumzeylanicum*) and Bay Leaf (*Syzygiumpolyanthum*) and Their Combination as Antidiabetic in Vivo

Shella Syahfitri*[1], Jansen Silalahi[2], Hotnida Sinaga[3]

[1] Department of Food Science, Faculty of Agriculture, Universitas Sumatera Utara, Medan, Indonesia
[2] Department of Pharmacy Biologi, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia
[3] Department of Food Science, Faculty of Agriculture, Universitas Sumatera Utara, Medan, Indonesia

A B S T R A C T

Diabetes Mellitus (DM) is a chronic disorder of carbohydrate (glucose) metabolism in the body and its prevalence is getting higher. Until 2015, 10 million cases of DM were found in Indonesia and allegedly continue to increase. Currently, the Indonesian government encourages people to consume traditional medicines because they remember the low side effects. Cinnamon (Cinnamomumzeylanicum) contains antioxidants that can reduce the risk of oxidative stress, a condition that is a major risk factor for several chronic diseases, including diabetes. Bay leaf (Syzygiumpolyanthum) also contains flavonoids that can lower glucose levels. Thus, cinnamon and bay leaves have the potential to be products that are beneficial to the community, namely diabetic herbal medicine. The purpose of this study was to determine the antidiabetic activity of cinnamon bark extract (Cinnamomumzeyl anicum) and bay leaf extract (Syzygiumpolyanthum) against reducing blood sugar levels in test animals.

This study used experimental methods in vivo. Using 28 alloxan-induced male mice were divided into 7 groups: (1) Negative control without treatment, (2) Positive control given metformin 45mg/kgBB, (3) Cinnamon dose 750 mg/kgBB, (4) Bay leaf 750 mg/kgBB, (5) Combination of Cinnamon and Bay Leaf dose ratio 1: 1 (375 mg/kgBB), 1: 2 (250 mg/kgBB and 500 mg/kgBB), and 2:1 (500 mg/kgBB and 250 mg/kgBB), given orally for 14 days. The results showed a percentage decrease in blood sugar levels during the test obtained Metformin administration 32.27%, cinnamon by 24.52%, bay leaf 21.05%, combination (1: 1) 23.71%, (1: 2) 35.83%, (2: 1) 40.83%.

Keywords: cinnamon, bay leaf, antidiabetic activity, in vivo

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*Address for Correspondence:
Shella Syahfitri, Department of Food Science, Faculty of Agriculture, Universitas Sumatera Utara, Medan, Indonesia

INTRODUCTION

Diabetes Mellitus (DM) or better known in the community as diabetes is a group of metabolic diseases with blood sugar levels that are above normal (hyperglycemia) due to impaired insulin secretion, insulin work or both [1].Hyperglycemia causes autooxidation of glucose, glycation of proteins, and activation of polyol metabolic pathways that accelerate the formation of reactive oxygen compounds (*Reaction Oxygen Species*: *ROS)*. The formation of ROS can increase the modification of lipids, DNA, and proteins in various tissues. Molecular modifications in various tissues result in an imbalance between antioxidant defenses and free radicals. This is the beginning of oxidative stress (oxidative stress), which is the situation if the capacity of ROS and free radicals is greater than that of antioxidants [2].Increased oxidative stress can be inhibited by antioxidants. Antioxidants are free radical blockers that work by donating electrons to free radicals and inhibiting the chain reaction of free radical formation. Efforts to increase antioxidant defenses to inhibit increased oxidative stress can be done by increasing antioxidants from outside the body. Non-nutritional compounds in foodstuffs can act as antioxidants, such as phenol compounds, polyphenols, and flavonoids [3, 4, 5, 6].Cinnamon contains cinamaldehid, eugenol, cinnamic acid, catechins, epicatechins, and other polyphenolic compounds. These phytochemical compounds make cinnamon potential as an antioxidant [4]. Bay leaf has the

ability as an astringent, which can precipitate mucous membrane proteins and form a layer that protects the intestine, thus inhibiting glucose intake which results in a decrease in blood glucose [6].Seeing some of the side effects resulting from chemical drugs, traditional medicine is a solution to reduce the side effects produced. The Indonesian government currently encourages people to consume traditional medicines because they remember the low side effects. [7].

MATERIALS AND METHODS

The materials used in this study were cinnamon (*Cunnamomum zeylanicum*) and bay leaf (*Syzygium polyanthum*) obtained from the city of Medan. Test animals of male *white musmusculus* mice aged 2-3 months with a body weight of 20-30 grams. The chemicals used are Alloxan monohydrate, Ethanol 96%, and Metformin.The tools used in this study were animal scales (*triple beam* balance), electrical balance (precisa), cage, a set of infundation extraction tools, oral syringes, 1 ml syringes, glucostest, micropipettes (socorex), scapel, rotary evaporator (stuart), rat holders, and glass tools (pyrex).

RESEARCH DESIGN

This research was conducted using experimental methods *in vivo*. Cinnamon extract and bay leaf and their comparison in the combination test as the independent variable, and blood sugar levels as the dependent variable. This study used a factorial Complete Randomized Design (RAL) with 2 factors. The first factor is the testing group and the second factor is the testing time. Each treatment will be done 4 times.

Factor 1 : Test Group (K)

K_1 = Negative control

K_2 = Positive control (methformin)

K_3 = Cinnamon

K_4 = Bay leaf

K_5 = Cinnamon : bay leaf (1:1)

K_6 = Cinnamon : bay leaf (1:2)

K_7 = Cinnamon : bay leaf (2:1)

Factor 2: Test time (days) (W)

W_1 = 3

W_2 = 7

W_3 = 14

Experimental Animal Adaptations

Test mice were first acclimatized with the environment and feed for one week in the laboratory before alloxane injection while observing their health, fed 2 times a day. The food of mice is pellets, while for drinking is given tap water.

Making 96% Ethanol Extract of Cinnamon (*Cinnamomum zeylanicum*) and Bay Leaf (*Syzygium polyanthum*)

The preparation of ethanol extracts of cinnamon (*Cinnamomum zeylanicum*) and bay leaf (*Syzygium polyanthum)* begins using maceration methods. In this filtering process, 96% ethanol solvent is used. Ethanol solvent was chosen because ethanol is a polar solvent whose use tends to be more universal. The residue and filtrate are separated and concentrated with a Rotary Evaporator at 48°C to produce a viscous extract [8].

Induction of alloxane in mice

Test animals induced alloxane monohydrate at a dose of 150 mg / kg body weight [9]. Reconstituted alloxane monohydrate should be injected immediately before it changes color from pink to clear. The dose of alloxane given to standard mice (30 g) is 30 g / 1000 g x 150 mg / kg body weight = 4.5 mg / 30 g body weight mice. Blood glucose measurements were taken before alloxane-induced mice (GD0). On the third day, fasting blood glucose levels were measured again when they had increased >140 mg / dL declared to have diabetes (GD3) and immediately given oral treatment of bay leaf and cinnamon extract [10,11].

Antidiabetic Activity Test

Testing antidiabetic activity according to the method described by [12], Animals were divided into seven groups namely variations of cinnamon extract (*Cinnamomum zeylanicum)*), bay leaf extract (*Syzygium polyanthum*), combination of cinnamon and bay leaf, negative control (no treatment), and positive control (Metformin). Each group consisted of 4 male mice which were divided into 7 groups each given: (1) Negative control (No treatment), (2) Metformin 45 mg/kgBB as positive control, (3) Cinnamon (*Cinnamomum zeylanicum*) dose 750 mg/kgBB, (4) Bay leaf (*Syzygium polyanthum*) dose 750 mg/kgBB, (5) Combination of Cinnamon and Bay Leaf dose comparison 1: 1 (375 mg/kgBB), 1 : 2 (250 mg/kgBB and 500 mg/kgBB), and 2 : 1 (500 mg/kgBB and 250 mg/kgBB), which are given orally.

Then each group was induced alloxane intraperitoneally. On the third day a blood sample is taken (initial). Then each group was given their own treatment. Therapy is given for 14 days orally. On days 3(H0), 7(H7), and 14(H14) fasting blood glucose levels were measured [13].

Data Analysis

Calculationof percentage (%) increase in blood glucose levels of the test group:

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

P = Blood Sugar Level after alloxane induction

Q = Baseline Blood Sugar Level

1. Calculation (%) of decrease in blood glucose levels of the test group:

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

P = Blood Sugar Level after alloxane induction

Q = Blood Sugar Level 14 days after treatment

RESULTS AND DISCUSSION

96% Ethanol Extract Yield of Cinnamon (*Cinnamomum zeylanicum*) and Bay Leaf (*Syzygium polyanthum*) Making ethanol extracts of cinnamon (*Cinnamomumzeylanicum*) and Bay Leaf (*Syzygium polyanthum*) using maceration method. In this filtering process, 96% ethanol solvent is used. The residue and filtrate are separated and concentrated with a Rotary Evaporator at a temperature of 48oC to produce a thick extract, and the yield obtained from the extraction of cinnamon (*Cinnamomum zeylanicum*) is 13.9% and bay leaf (*Syzygium polyanthum*) 13.8%.

Percentage increase in blood sugar levels after alloxane induction

Table 1: Average value of Percentage (%) increase in Blood Sugar Levels in mice after alloxane induction

*Test Group (K)	Average Blood Glucose Level (mg/dl) ± SD		Percentage Increase (%)
	Before	After Aloxane induction	
1	104,25 ± 7,14^{abc}	192,00 ± 9,66^{abc}	84,44
2	104,50 ± 7,05^{abc}	186,00 ± 7,87^{abc}	78,80
3	100,00 ± 3,83^{a}	318,25 ± 140,43^{gh}	219,88
4	107,50 ± 5,20^{abc}	235,00 ± 60,24^{abc}	120,81
5	102,75 ± 7,27^{abc}	253,75 ± 73,87^{def}	145,77
6	101,25 ± 4,65^{ab}	321,50 ± 134,78^{gh}	214,09
7	105,50 ± 5,51^{abc}	351,25 ± 123,32^{h}	233,83

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

*Test Group: 1= Negative control (no treatment) 2= Positive control (metformin) 3= Cinnamon 4= Bay leaf 5= Cinnamon:bay leaf (1:1) 6= Cinnamon:bay leaf (1:2) 7= Cinnamon:bay leaf (2:1)

Mice that will be used previously in alloxane induction at a dose of 150 mg / KgBB. This induction is useful for increasing diabetes levels in mice so that it can be categorized as hyperglycemia mice. Mice are expressed in a diabetic state when the average blood sugar level ≥ 140 mg / dl [8].

The Effect of Cinnamon Extract (Cinnamomum zeylanicum) and Bay Leaf (Syzygium polyanthum) Treatment and Their Combination on Reducing Blood Sugar Levels of Mice

The decrease in blood sugar levels of mice during treatment, namely days 3, 7, and 14 days can be seen in Table 2 and Table 3.

Table 2: Blood Sugar Levels (mg/dl) in mice during testing

* Test Group (K)	Test Time (days) (W)		
	3	7	14
1	263,75 ± 49,08^{cd}	282,50 ± 32,34^{de}	339,00 ± 50,15^{f}
2	168,00 ± 5,10^{ab}	145,50 ± 5,00^{ab}	125,75 ± 7,63^{a}
3	306,75 ± 139,71^{de}	272,25 ± 116,59^{de}	240,00 ± 109,61^{cd}
4	219,00 ± 51,40^{ab}	196,50 ± 37,70^{ab}	182,50 ± 34,26^{ab}
5	228,25 ± 46,42^{ab}	200,50 ± 32,96^{ab}	189,00 ± 33,93^{ab}
6	257,50 ± 101,24^{cd}	231,75 ± 98,80^{ab}	203,25 ± 76,39^{ab}
7	272,00 ± 81,91^{de}	233,00 ± 64,02^{ab}	198,50 ± 48,82^{ab}

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

*Test Group: 1= Negative control (no treatment) 2= Positive control (metformin) 3= Cinnamon 4= Bay leaf 5= Cinnamon:bay leaf (1:1) 6= Cinnamon:bay leaf (1:2) 7= Cinnamon:bay leaf (2:1)

Based on the table above, it can be seen that overall administration of cinnamon extract and bay leaf can reduce blood sugar levels during treatment as according to [14], this is due to suspected a number of bioactive compounds that have antidiabetic activity in cinnamon, as described in research [15], states that cinamaldehid has biological activity as an antioxidant, antiviral, antifungal and antibacterial. So synamaldehid significantly lowers blood sugar levels, increases sensitivity and improves insulin [16].

The main flavonoid content in bay leaf ethanol extract is quercitrin and fluoretin which also function as antioxidants [17]. In patients with DM there is an increase in the number of free radicals because they are produced in the body in an unbalanced state. Flavonoids that have an effect as antioxidants that act as an antidote to free radicals such as Reactive Oxygen Species (ROS) [18,19]. Flavonoids work by inhibiting the reabsorption of glucose from the kidneys [20], regulating the work of enzymes involved in carbohydrate metabolism pathways, increasing insulin secretion. . Many

people use it to lower blood glucose levels in people with diabetes mellitus. The percentage decrease in mouse blood sugar levels during the 14-day testing period can be seen in Table 3.

Table 3: Percentage Decrease in Blood Sugar Levels (%)

* Test Group (K)	Test Time (days) (W)		
	3	7	14
1	36,87 ± 19,62^{bc}	46,97 ± 12,73^{b}	76,38 ± 23,23^{a}
2	-9,56 ± 4,59^{cd}	-21,68 ± 4,10^{cd}	-32,27 ± 5,67^{hi}
3	-3,93 ± 1,65^{c}	-14,18 ± 1,25^{cd}	-24,52 ± 4,36^{ef}
4	-6,34 ± 3,73^{cd}	-15,24 ± 6,82^{cd}	-21,05 ± 8,46^{cd}
5	-8,39 ± 8,53^{cd}	-18,87 ± 10,37^{cd}	-23,71 ± 9,05^{de}
6	-18,86 ± 8,89^{cd}	-27,69 ± 6,88^{gh}	-35,83 ± 5,23^{jk}
7	-21,05 ± 6,09^{cd}	-17,71 ± 34,81^{cd}	-40,83 ± 11,17^{l}

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

*Test Group: 1= Negative control (no treatment) 2= Positive control (metformin) 3= Cinnamon 4= Bay leaf 5= Cinnamon:bay leaf (1:1) 6= Cinnamon:bay leaf (1:2) 7= Cinnamon:bay leaf (2:1)

Table 3 shows that in each treatment group there was an increase in the percentage of decrease in blood sugar levels, but in group 1 did not experience a percentage decrease but increased to 76.38%, this is because group 1 was not given any treatment after alloxane induction In the results of this study, the antidiabetic activity of cinnamon extract was higher than bay leaf extract, this was shown in the percentage decrease in blood sugar levels from cinnamon dose of 750 mg/kgBB of -24.52% while bay leaf dose of 750 mg/kgBB of -21.05%. In the test group of the combination of cinnamon and bay leaf with a ratio of (2: 1) dose of 500 mg / kg body weight: 250 mg / kg body weight is the test group with the highest percentage of reduction in blood sugar levels of -40.83%. Mice given metformin as a comparison with a dose of 45 mg / kg body weight were also effective in reducing blood sugar levels, namely the percentage decrease of -32.27%.

CONCLUSION

Based on the results of the study, it can be concluded that cinnamon extract (Cinnamomumzeylanicum) has higher antidiabetic activity compared to bay leaf (Syzygiumpolyanthum), which is -24.52% while bay leaf is -21.05% and the best combination is cinnamon extract (Cinnamomumzeylanicum) and bay leaf (Syzygiumpolyanthum) with a ratio of 2: 1 (500: 250 mg / kg BB) with a percentage decrease in mouse blood sugar levels -40.83%.

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