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RESEARCH ARTICLE

Effect of *Coriandrum sativum* L on Blood Glucose Levels among Alloxan-Diabetic Mice (*Rattus norvegicus strain wistar*)

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ABSTRACT:
The blood glucose level of the body tends to increase slightly after the age of 50. The coriander (*Coriandrum sativum L*) is a member of the Apiaceae family and it grows in a wide range conditions and can be used as antidiabetic. The purpose of this study was to determine the effect of coriander water extract on the blood sugar levels of white rats (*Rattus norvegicus strain wistar*). The method of this study involved experimental animals, specifically 20 *Rattus norvegicus strain wistar* ranging from 150-200grams with an age between 2-3 months. The mice were injected with an alloxan solution to induce a diabetic condition and then they were divided into four groups and treated. The treatments were 0.5% Na CMC, glibenclamide 0.45mg/Kg b.w, coriander extract of 100mg/Kg b.w and coriander extract of 200mg/Kg b.w for 15 days. The blood glucose level of the mice was measured on days 0, 1, 5, 10 and 15. The results showed that the 0.5% CMC placebo had no effect in terms of reducing the glucose level of the rats, Glibenclamide 0.45mg/Kg b.w had an effect in terms of reducing the blood glucose level, as did coriander extract 100mg/Kg b.w and 200mg/Kg b.w among the alloxan-diabetic mice.

KEYWORDS: Diabetic, Blood glucose, Coriander seed, Mice, Alloxan.

INTRODUCTION:
The blood sugar refers to the concentration of glucose in the blood which is strictly regulated by the body[1]. Blood sugar is the main source of energy for body cells[2]. A fasting blood glucose level is 4-8 mmol/L/day[3], this level increases after eating and the lowest level in the morning before consuming food or breakfast[4].

The blood glucose levels tend to increase slightly after the age of 50[5], especially in people who are inactive[6] and obese[7]. An increase in blood glucose levels after eating or drinking stimulates the pancreas to produce insulin, thus preventing a further increase in blood glucose level and causing the blood glucose levels to decrease slowly is a positive[4].

The coriander (*Coriandrum sativum L*) is a member of the Apiaceae family and grows in a wide range of conditions[8]. It is commonly used as medical plant[9]. Benefits could be obtained from the leaves, seeds and fruits[10]. Coriander seeds are a strong flavorful spice used as an ingredient in cooking and food flavoring[10]. The most widely used part is seed[11,12]. There have been many studies on the efficacy of coriander in relation to being anti-fertility, anti-diabetic, anti-hyperlipidemia[13], antioxidants, anti-convulsant and antifungal[9,14,15], anti-inflammatory[16], antibacterial[17] and to prevent leucorrhoea among women[18]. The chemical compounds in coriander are quercetin 3-glucoronide[19], linalool, camphor, geranyl acetate, geraniol[20] and coumarins[21]. The aim of this study to test the anti-diabetic activity of coriander water extract using the glucose tolerance test method.

Based on this background, this study went on to measure the effect of coriander on blood sugar levels. The results describe the effect of coriander water extract on blood sugar level. Furthermore, coriander can be a potential natural ingredient source that is able to decrease high blood sugar levels.

MATERIAL AND METHODS:
All of the protocols of this study were approved by the ethical committee board from Universitas Muhammadiyah Banjarmasin, Indonesia (Number

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019/UMB/KE/II/2020. We followed the required standards for care as well as the protocols on the use of experimental animals. The mice were housed in a proper cage and were fed a standard commercial pellet diet.

Instruments:
The instruments used in this study were surgical instruments, maceration vessels, rotary evaporators, waterbaths, ovens, and a mouse cage. In addition, the materials used were laboratory male wistar mice (*Rattus norvegicus strain wistar*) weighing 150-200grams aged between 2-3 months, rat feed, coriander, ethanol, filter paper, diethyl ether, aqua pro injection 70%, alloxan, Na CMC, cotton, sterile gloves, sterile gauze, and plaster.

Plant Preparation and extraction:
The coriander seeds were collected from the local market in Martapura, Kalimantan (Borneo island). One kg of coriander seeds was dried using an oven for 24 hr at 60°C to get simplicia. The simplicia was blended for 1 minute until smooth, then 100grams of the smooth simplicia was extracted by maceration using 1L of sterile aqua for 6 hr on a hotplate and stirred every 1hr. The solvent of the smooth simplicia was evaporated using a rotary evaporator and incubated using a water bath until a thick extract was obtained.

Experimental animals, protocols, and experimental layout:
The experimental animals used were 20 *Rattus norvegicus strain wistar* weighing 150-200grams aged between 2-3 months. The mice were injected with a solution of alloxan. The alloxan dose was 150mg/kg body weight[22], so for each mouse with a 200grams body weight, they were dosed with 30mg of alloxan. We prepared 30mg alloxan in 1mL of sterile aqua. After 24 hours, the blood glucose of mice was measured through a tile vine. The mice displaying hyperglycemia were chosen for the experiment.

The mice were randomly divided into four groups. There were five mice in each group and they were treated as follows:
Group I (Negative control group) received CMC (carboxymethylcellulose) 0.5%, once a day for up to 14 days.
Group II (Positive control group) received glibenclamide 0.45 mg/kg bodyweight, once a day for up to 14 days.
Group III received coriander extract 100 mg/kg bodyweight, once a day for up to 14 days.
Group IV received coriander extract 200 mg/kg bodyweight, once a day for up to 14 days.

Fasting Blood Glucose Level:
Blood glucose level was measured after 12 hours fasting on 15th day using a one touch glucometer.

RESULTS AND DISCUSSION:

Simplicia:
Simplicia is a dry material that has not undergone processing and is used for treatment[23]. The simplicia powder in this study was made from dried coriander seed. The simplicia was tested using an organoleptic technique involving the sensory organs. The aim was to determine the macroscopic description of the natural material. Table 1 showed the results of the organoleptic qualities of the simplicia.

Table 1. The results of the organoleptic qualities of the simplicia

Coriander Weight (Fresh Material)	Dry Weight (Simplicia)	Organoleptic
1000 gram	800 gram	Smell: Typical Coriander Taste: Bland, slightly bitter Color: Yellowish Form: Powder

The results showed that 1000grams of dried coriander seed was used to obtain 800grams of simplicia powder. The shrinkage of the fresh coriander happened due to coriander containing water on the surface that was removed during the washing process before treatment. The water can interfere with the storage life. It is important to dry it at a temperature of no more than 60° C.

Drying is different for each material. It depends on the part of the plant used and the characteristics of the material. Drying time also depends on the wetness of the sample[24]. Drying for too long will cause damage to the active ingredients. The parameters of ideal drying can be evaluated according to the physical appearance of the material[24]. Dried materials are called simplicia. Simplicia has a long life duration of 3- 6 months, depending on the storage technique[23].

The organoleptic evaluations were that the simplicia smell was typical of coriander, the taste was bland and slightly bitter, the color was yellow, and the form was that of a powder. Simplicia has a distinctive smell because it contains an essential oil[25]. The essential oil is classified as a terpenoid[26]. Coriander seed contains 60-70% linaool, geraniol (1.6-2.6%), geranil aceta (2-3%), camphor (2-4%), and hydrocarbon groups such as α-pinen, β-pinen, dipenten, p-simene, α-terpinen and γ-terpinen, terpinolene and fellandren (20%)[27,28]. The smell of coriander powder is stronger than that of coriander seeds. The coriander seed is covered with a cell layer that functions to prevent the loss of the essential oils[29]. Coriander powder has a yellowish color. This coloration can turn brown if the drying process is undergone for too long. The taste is slightly bitter, similar to the taste of orange seeds. The powder simplicia form will facilitate the extraction. The small particle makes the extraction process optimal.

Extraction process:

Table 2 showed the results of the extraction and the organoleptic evaluation of the extract

Table. 2: Results of the extraction process and organoleptic tests

Coriander simplicia	Thick extract	Rendemen	Organoleptic
800gram	24.75 gram	3.09%	Smell: Typical Coriander Taste: A bit bitter Color: Dark brown Form: Semi-Solid

The results of the extraction showed that 800grams of coriander extract was obtained in a thick form totaling 24.75grams. The percent yield of the extract was 3.09%. These results indicate that 3.09 out of the 100 parts of the sample were extracted. These results can be used as a reference in order to estimate the required coriander sample.

The organoleptic test results showed that the extract had the distinctive smell of coriander, a slightly bitter taste, was dark brown in color and had a semisolid form. The smell of the extract is similar to that of coriander powder. The smell comes from essential oils found in the natural ingredients[25,30]. The slightly bitter taste of the extract is due to the concentrated content of the active ingredients. The taste is different from that of coriander powder (simplicia). Coriander powder has no taste because it is dominated by the cell membrane. In the extract, the cell membrane has already separated[31]. The form of coriander extract is semisolid. The semisolid form contains very little water, minimizing the potential for a microbial presence. It is also relatively stable and can generally stand for up to 6 months in suitable storage. Extract storage should be done in a refrigerator which has a temperature of 4 - 10°C[31].

Activity test:

The alloxan damaged the mice's pancreas and the mice became diabetic. The diabetic mice that had increased blood glucose levels were assigned to a group; a negative control group (CMC), positive control group (glibenclamide) and two coriander extract groups with two different concentrations (100mg/kg b.w and 200 mg/kg b.w). Carboxymethyl Cellulose Sodium (Na CMC) is a suspension agent. It assisted the extract by dissolving it in sterile aqua. It was used as a placebo in the negative control group. Na CMC was also a solvent in glibenclamide. Glibenclamide is a sulfonylurea of the diabetic medication class. It stimulates insulin secretion from the pancreas[11]. In addition, the pancreases of the mice were stimulated by glibenclamide to produce insulin normally.

The coriander extract groups were in order to give two different doses to see the efficacy of said doses. The treatment for each group was given on the 1st to the 14th day and the treatment was given orally using a pipe. Table 3 showed the results of the measurement of the blood glucose levels among the sample mice.

Table 3: The blood glucose level among the mice in each group

Treatment	Mice Code	Blood Glucose Level (mg/dl*)				
		Before alloxan induced	Day-1	Day-5	Day-10	Day-15
NaCMC 0,5% (Negative control group)	1	95	145	144	142	139
	2	98	152	150	148	145
	3	102	148	148	145	139
	4	94	152	150	147	144
	5	96	149	147	139	138
	Mean	**97±1.72**	**149.2±1.54**	**147.8±1.97**	**144.2±4.25**	**141±1.92**
Glibenclamide (Positive control group)	1	93	158	135	95	95
	2	104	152	125	108	106
	3	98	148	119	99	98
	4	95	147	136	96	95
	5	99	151	138	105	102
	Mean	**97.8±1.72**	**151.2±1.54**	**130.6±1.97**	**100.6±4.25**	**99.2±1.92**
Coriander extract 100 mg/kg b.w	1	93	147	140	135	105
	2	89	154	138	133	110
	3	96	155	137	130	98
	4	95	148	140	138	98
	5	94	156	139	136	99
	Mean	**93.4±1.72**	**152±1.54**	**138.8±1.97**	**134.4±4.25**	**102±4.25**
Coriander extract 200 mg/kg b.w	1	104	149	138	108	102
	2	101	151	140	107	98
	3	94	150	139	101	96
	4	92	153	141	105	95
	5	98	149	138	99	98
	Mean	**97.8±1.72**	**150.4±1.54**	**139.2±1.97**	**104±4.25**	**97.8±4.25**

*) Normal blood glucose for mice: 50 – 135 mg/dl, hyperglycemia level for mice: 143 – 161 mg/dl

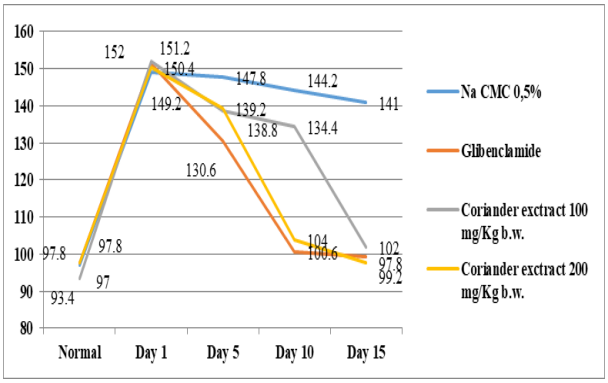

Fig 1: Blood glucose level among the mice

Table 3 and figure 1 showed that at the beginning of the measurement period, the blood glucose level of the mice was in the normal range (50 - 135mg/dl). The mice were induced with alloxan to make them diabetic. The next day, we measured their blood glucose levels. The mice

were treated according to their designated group. On the 5th day, there was a decrease in blood glucose level in the positive control group as well as in one of the coriander extract groups (glibenclamide 100 mg / Kg b.w extract, and 200mg/Kg b.w). However, the greatest decrease in blood glucose level was found in the positive control. This result is similar to the previous studies on glibenclamide, which is a drug that has a specific mechanism for decreasing blood glucose level[32-34].

On the 10th day, the results showed that the blood glucose levels were in the normal for both the positive control group (glibenclamide) and one of the coriander extract groups (200mg /kg b.w). For the other coriander extract group (100mg/kg b.w), the results showed that the blood glucose level also decreased but this did not occur in all mice in the group.

On the 15th day of measurement, it was found that one coriander extract group (100mg/kg b.w) could decrease the blood glucose level into normal range. In the positive control and coriander extract group of 200mg/ kg b.w, there was no change in the blood glucose levels after day 10. In the negative control group, there was a decrease in the blood glucose level. However, it was not significant and still in the hyperglycemic range. The previous study mentioned that 500mg/kg b.w of coriander extract was needed per day to reduce the blood glucose levels of the mice[35], and that coriander was effective at decreasing the blood glucose level of diabetic rats[30].

The Shapiro-Wilk normality test showed that the data was normally distributed ($p > 0.05$) and that the data was homogenous. There we used the One Way Anova test. The analysis showed that on day 5, the blood glucose levels in the positive control group (glibenclamide) showed significant differences compared to the other groups. Glibenclamide is the main drug to decrease the blood glucose level and it has fast activity. The analysis also showed that the coriander extract groups of 100mg /Kg b.w and 200mg/Kg b.w were the same. On the 5th day, the benefits of using natural ingredients were not seen. Natural ingredients do not have an immediate effect and the use of these ingredients must be continued for several weeks. All natural ingredients work according to these principles[36].

The analysis showed that on the 10th day, there was no significant difference in terms of blood glucose level between the positive control group and the 200mg/Kg b.w extract groups. The results showed that the blood glucose levels reached normal levels. In the 100mg/Kg b.w extract group, the blood glucose levels also decreased but differently to the positive control group and the 200mg coriander extract group. In the negative control group, the blood glucose levels were still very high and significantly different from the others group. This study was similar with previous studies that herbal had effect on diabetes[37-40].

The analysis showed that the 15th day indicates that there was no significant difference between the positive control group (glibenclamide) and the 200mg/kg b.w and 100mg/kg b.w extract of coriander groups. The results showed that the three treatments decreased the blood glucose level on the 15th day. It additionally showed that the two strengths of coriander extract had an effect as an antidiabetic in terms of decreasing the blood glucose level[9,14,15].

The results showed that the 0.5% CMC placebo had no effect in terms of reducing the blood glucose levels in the rats, Glibenclamide 0.45mg/Kg b.w had an effect and the coriander extract 100mg/Kg b.w and 200mg/Kg b.w had an effect when it came to decreasing the blood glucose level of the alloxan-diabetic mice.

CONCLUSION:

The study showed that 0.5% CMC placebo had no effect on reducing the blood glucose levels in the rats. However, the other treatment groups had effect on reducing the blood glucose levels in the rats. The significant effect group was the group IV that received coriander extract 200 mg/kg bodyweight for up to 14 days, it had the similar ability as the diabetes mellitus medicine, namely glibenclamide.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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