

Comparison of Antidiabetes Effects of Single Black and Mixed Black Cumin Products on Reduction of Blood Glucose Male White Mice

1st Mona Rahmi Rulianti
Pharmacy Departement
Poltekkes Kemenkes Palembang
Palembang,Indonesia
monarahmi@poltekkespalembang.ac.id

2nd Vera Astuti
Pharmacy Departement
Poltekkes Kemenkes Palembang
Palembang,Indonesia
vera@poltekkespalembang.ac.id

Corresponding author: monarahmi@poltekkespalembang.ac.id

Abstract-Black Cumin (*Nigella sativa*) has long been known to be efficacious in curing diseases. Many studies that prove Black Cumin or better known in the community by the name Black Seed can be efficacious as an immunomodulator, antibacterial, anti-inflammatory antioxidant and as an antidiabetic. Black Cumin or better known by the trade name Habbatusauda has been widely circulating in the market, both in the form of dry or oil in drug stores and pharmacies so it is easy to obtain. Some of these Habbatusauda products can be found in a single form or in combination with other oils such as a mixture of Habbatusauda oil with Soursop leaf extract, and in the form of a mixture of Habbatusauda oil with Olive oil. This research is an experimental study with a pretest and post test with control group design. This study used 24 white male Wistar which were divided into 6 groups randomly. Group I as a negative normal group. Group II as a positive control group. Group III was given a single black cumin oil dose of 3.9 mg / 20 gram/day. Group IV was given black cumin oil mixed with soursop leaves at a dose of 3.9 mg / 20 grams/day. Group V was given black cumin oil mixed with olive oil at a dose of 3.9 mg / 20 grams/day. Group VI was given Metformin 65 mg / kg / day. The study was conducted for 11 days where alloxan was injected on the 3rd day. Blood sampling is done on the 2nd, 6th, and 11th day and the glucose levels are examined using the Easy Touch® brand Glucotest. The data obtained were analyzed statistically with One Way Anova and continued with Post Hoc Tests using the SPSS 16.0 for Windows Evaluation Version program. One Way Anova results on decreasing blood glucose levels between treatment groups showed a significant difference with $p: 0,000$ or $p < 0.01$. Post Hoc Tests results showed a significant difference $p: 0,000$ or $p < 0.01$ group II with groups III, IV, V, VI.

However, there were no significant differences from groups III, IV, V in the decrease in blood glucose levels of $p: 0.018$ or $p > 0.01$. From the results of this study it was found that a single black cumin oil, black cumin oil mixed with soursop leaves and olive oil black cumin oil have the same effect in decreasing the blood sugar levels of alloxan-induced male white mice.

Keywords: Black Cumin, soursop leaf, olive oil, hyperglycemia, antidiabetic.

I. INTRODUCTION

Proving the benefits of traditional medicine through clinical trials supported by immunological research, both through qualitative and quantitative assessments, needs to be encouraged (Djauzi, 2003). *Nigella sativa* is a species of the *Nigella* genus which has approximately 14 plant species belonging to the Ranunculaceae family. This plant comes from Southern Europe, North Africa, and South Asia. Other names for *Nigella Sativa* include: Kalonji (Hindi), Kezah (Hebrew), Chamushka (Russian), Habbatus Sauda (Arabic), Siyah daneh (Persian), Fennel Flower / Black Caraway / Nutmeg Flower / Roman Coriander / Black Onion Seed (English), or Jintan Hitam (Indonesia) [1].

The processed products of black cumin have been widely marketed in Indonesia, in the form of oil, seeds, extracts and so on. Some people have long known the black cumin product under the brand name Habbatusauda, easily available in the market at an affordable price. Apart from being single, this Black Seed product is also combined with soursop leaves and olive oil. Black cumin seeds or powder currently traded

are usually packaged in capsules or black cumin oil in bottles [2].

The biological activity of black cumin seeds has been widely reported such as anthelmintic, antibacterial, anti-inflammatory, anti-tumor, antioxidant, immunomodulatory, diuretic, antihypertensive, anti-diabetic, anti-plasma, pulmonary disease drug, and anti-arthritis [3].

Diabetes mellitus is a multifactorial disease, characterized by chronic hyperglycemia syndrome and disorders of carbohydrate, fat and protein metabolism caused by insufficient insulin secretion or insulin endogenous activity or both [4]. Hyperglycemia that is not controlled can also cause many complications such as neuropathy, stroke and peripheral vascular disease [5].

II. METHOD

This type of research is experimental with a pre and post control group research design. The research is planned to be carried out at the Pharmacology Laboratory of the Department of Pharmacy, Poltekkes Palembang in August - September 2018. This study used male Wistar mice (*Mus musculus L.*) 3 months old and 20-35 grams, as many as 24 divided into 6 (six) groups. Sample selection is done by simple random technique (Sample Random Sampling).

The treatment group in this study consisted of:

- G1 : negative control, namely the group without treatment
- G2 : positive control, namely the group of mice induced by alloxan 160 mg / kg BB intraperitoneal
- G3 : the group of mice induced by alloxan 160 mg / kg BW intraperitoneal on day 3, then on day 6 were given Habbasyi Oil 3.9 mg / 20 g BW for 5 days
- G4 : group of mice induced by alloxan 160 mg/ kg BW intraperitoneal on day 3, then on day 6 were given Habbat Plus soursop leaf oil 3.9 mg / 20 g BW for 5 days
- G5 : the group of mice induced by alloxan 160 mg / kg BW intraperitoneal on the 3rd day, then on the 6th day they were given Black Seed Oil Plus Olive Oil 3.9 mg / 20 g BW for 5 days.
- G6 : the group of mice induced by alloxan 160 mg / kg BW intraperitoneal on the 3rd day, then on the 6th day they were given Metformin 65 mg / BW for 5 days.

The data obtained were analyzed statistically with the One Way Anova test with $p = 0.01$ and continued with

the Post Hoc Test using the SPSS program. One Way Anova was used to determine whether the mean of the five treatment groups in this study was significantly different. Meanwhile, the Post Hoc Test was used to determine the mean pairs that differed the most between groups.

III. RESULTS

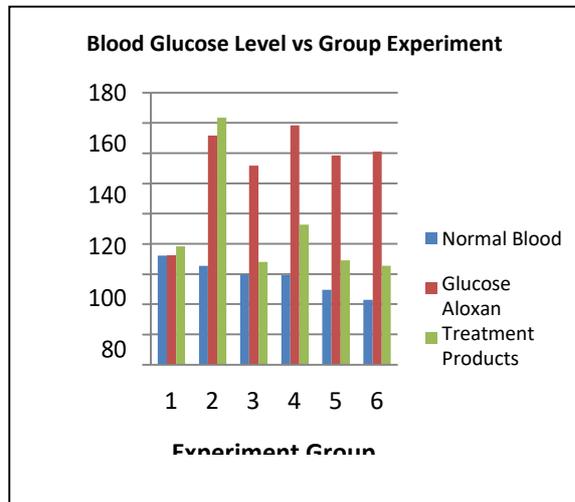
A. Measurement of blood glucose level

In this study, the measurement of blood sugar levels of male white mice was carried out three times using the Easy Touch® glucometer test. Measurement of blood sugar levels was carried out at the beginning of the experiment before the treatment was carried out, then measurements were carried out after being induced by Aloxan to see the hyperglycemic / diabetes status in mice, and measurement of blood sugar levels after being given treatment, namely given Habbatusauda Oil in single form, Habbatusauda oil a mixture of soursop leaves, and oil. Habbatusauda olive oil mixture. Blood sugar levels were measured after the mice were fasted for 12 hours.

Table 1. Results of Blood Glucose Level of mice during treatment

Group	No Mice	Blood Glucose Level I (mg / dl)	Blood Glucose Level II (mg / dl)	Blood Glucose Level III (mg / dl)
I	1	73	66	84
	2	57	57	61
	3	82	76	85
	4	77	89	83
II	1	56	150	154
	2	82	154	162
	3	69	144	168
	4	55	158	170
III	1	49	115	62
	2	59	124	66
	3	72	134	76
	4	59	154	68
IV	1	79	158	78
	2	59	158	94
	3	59	183	102
	4	40	134	97
V	1	62	144	57
	2	39	140	76
	3	39	170	74
	4	58	100	69
VI	1	44	113	44
	2	39	102	87
	3	58	162	66
	4	31	187	65

Picture 1. Blood Glucose Level chart against the Experiment group



B. Results Analysis

1. Blood glucose levels after being given a single *Habbatusauda* oil, a mixture of soursop and olive leaves.

The results of the Levene statistical homogeneity test showed a result of 0.728 ($p > 0.01$) so that the data variance between groups was the same, therefore it could be tested using One Way Anova.

The One Way Anova test results showed 0.000 ($p < 0.01$), thus it was known that there was a significant difference in the mean in the six groups, so that it could be continued with the Post Hoc Test which showed differences in each group. Group II had significant differences with groups I, III, IV, V, VI after being given the treatment, namely giving *Habbatusauda* oil single, a mixture of olive oil soursop leaves, and Metformin.

2. Decreased Blood Glucose Levels in the Black Seed Single group, a mixture of Soursop Leaves, Olive Oil and Metformin

The results of the Levene statistical homogeneity test showed a result of 0.608 ($p > 0.01$) so that the data variance between groups was the same, therefore it could be tested using One Way Anova.

The One Way Anova test results showed a result of 0.018 ($p > 0.01$), thus it was known that there was no significant difference between the four groups, meaning that the administration of single cumin oil, a mixture of soursop leaves, olive oil, and metformin did not give a significant difference. The significant reduction in glucose levels means that the four groups have the same potential to reduce blood sugar levels.

IV. DISCUSSION

From the table, the results of measuring blood glucose levels in the table show that there are differences in the average blood glucose levels in each group before treatment (BGL I), after alloxan administration (BGL II), and after treatment (BGL III). The result BGL II measurement is higher than BGL I because alloxan administration causes an increase in blood glucose levels. After doing the Post Hoc Tests at KGD 2, the comparison between group I and groups II, III, IV, V, VI showed $p < 0.01$ results. Therefore, the increase in blood glucose levels after alloxan administration has a significant difference compared to the normal group that did not receive alloxan.

Alloxan is an oxidant agent that causes peroxidative damage to the pancreatic cell membrane. Pancreatic beta cells are sensitive to oxidative stress, so the presence of excessive levels of ROS causes a decrease in number *glutathione peroxidase* pancreas (GSH). This causes disruption of the redox status of pancreatic beta cells resulting in beta cell dysfunction. The resulting insulin levels drop resulting in an increase in blood glucose levels (hyperglycemia)[6].

After giving black seed oil, blood glucose levels in groups III, IV, V, VI decreased significantly ($p < 0.01$) compared to the control group. This means that the administration of single black cumin oil, a mixture of soursop leaves, a mixture of olive oil and metformin has a hypoglycemic effect or is able to reduce blood glucose levels. Followed by a Post Hoc Test which showed the differences in each group. Group II had significant differences with groups I, III, IV, V after being given treatment, namely giving *Habbatusauda* oil alone, a mixture of olive oil soursop leaves, and Metformin. This shows that giving black cumin oil single, a mixture of soursop leaves and a mixture of olive oil is effective in reducing blood glucose levels of mice to normal limits. *thymoquinone*, zinc (Zn), MUFA (monounsaturated fatty acids) and PUFA (polyunsaturated fatty acids).

From the results of group V, namely cumin oil and olive oil samples also showed a decrease in blood sugar levels in mice. In a previous study by researchers from Yuzinkwail University, Turkey, published in the magazine *Tohoku J Exp Med*, September 2003, conducted a study on 50 mice infected with diabetes mellitus by being given the substance streptozotocin in the peritoneum (stomach lining). The researchers found that giving black seed oil to mice with diabetes caused a decrease in blood sugar levels in these mice, as well as an increase in insulin levels in the blood. In addition, it also causes an increase the activity of beta cells in the pancreas which are responsible for secreting insulin. Meanwhile, in De Bruyne's book in 2008,

olive oil is an oil containing monounsaturated fatty acids as its main component. As the largest component, monounsaturated fatty acids in olive oil have benefits as nutritional therapy for people with diabetes mellitus. This is associated with increased insulin activity, namely increasing insulin sensitivity in the targeted tissue, increasing insulin secretion, and repairing pancreatic beta cells [6].

Furthermore, the One Way Anova test results in the treatment group showed 0.018 ($p > 0.01$) results, thus it was known that there were no significant mean differences in the four groups, meaning that the administration of single cumin oil, a mixture of soursop leaves, olive oil, and Metformin did not provide a significant difference in reducing glucose levels, meaning that the four groups had the same potential to reduce blood sugar levels.

V. CONCLUSIONS

A single product of Jinten Hitam, black cumin oil mixed with soursop leaves and black cumin oil mixed with olive oil has an anti-diabetic effect and can reduce blood sugar levels of alloxan-induced hyperglycemic mice comparable to Metformin ($p < 0.001$). There was no significant difference from product variants of single black cumin, black cumin oil mixed with soursop leaves, and black cumin oil mixed with olive oil in reducing blood sugar levels of mice ($p > 0.01$).

For further research, it is expected to measure the decrease in blood sugar levels of mice by varying the dosage of each dosage form of black cumin oil, either single or mixed.

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