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TEST THE EFFECTIVENESS OF GRAPE SEED EXTRACT AS AN ANTIDIABETIC DRUG IN MALE WHITE RATS WISTAR STRAIN

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ABSTRACT

The research aims to know the effectiveness of grape seeds in lowering blood sugar levels in white rats. The research began with grape seed extraction using the maceration method. The results of macerate were given to white rats that were given grape seed extract samples at doses of 75 mg/200 grams BW, 125 mg/200 grams BW, and 250 mg/200 grams BW. The positive control was metformin, and the negative control was given distilled water. All were given treatment for 14 days. On days seven and 14, a blood sugar test was carried out to assess the effectiveness of grape seed extract. The results showed that of the five treatment groups, sample group I (extract at a dose of 75 mg/200 gram BW) and sample group III (extract at a dose of 250 mg/200 gram BW) affected reducing blood sugar levels in rats. This is proven by comparing blood sugar levels after being given alloxan on the seventh day in the two groups, showing better results in reducing blood sugar levels than the other groups. It can be concluded that grape seed extract can properly reduce blood sugar levels in white rats with type II diabetes mellitus.

Keywords: Type-II Diabetes Mellitus, Grape's seed, Maceration, Albino Rats, Blood Sugar Level

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INTRODUCTION

The World Health Organization (WHO) explains that diabetes cases globally reached 415 million people in 2015. It has been predicted that in the next 30 years, the number of diabetes cases will increase significantly to reach 641 million people (Dankoly et al., 2023). According to WHO, type II diabetes mellitus is a chronic disease where the pancreas cannot produce enough insulin to regulate blood sugar levels or when the human body cannot use the insulin produced by the pancreas effectively. Glucose in the blood will result in uncontrollability. Damage will occur to certain body organs, such as the heart, kidneys, eyes, and nervous system (Galicia-Garcia et al., 2020; Prolanis et al., 2022).

In Indonesia itself, type II diabetes mellitus has succeeded in occupying the top five positions among the diseases most commonly suffered in Indonesia. In 2019, the IDF (International et al.) explained that Indonesia was in sixth position in the world, with an age range between 20-79 years, and had 10.3 million cases of people living with diabetes (Mulmuliana 1, 2022). According to Riskesdas, in 2013, East Java Province contributed 2.5% of cases of people suffering from type II diabetes mellitus. Cities in East Java that contribute the largest number of people suffering from diabetes mellitus include the cities of Surabaya, Malang, Lamongan, and Bangkalan (Tsalissavrina et al., 2018). A plant that has an important role as a solution in preventing type II diabetes mellitus is grapes.

It is believed that the ingredients in grapes can be used as an antidiabetic drug. The ingredients that have an important role in preventing diabetes are flavonoids. This content is generally found in

vegetables, fruit, and plant stems (Clara et al. et al., 2017; Arifin & Ibrahim, 2018; Khoirunnisa & Sumiwi, 2019; Azzahra et al., 2022; Kamilia et al. et al., 2022; Nofianti et al., 2022). Grape seeds also have similar contents in their fruit and leaves but are rarely used in daily life and are often thrown away by local people. This research hopes that not only grape leaves and fruit can be used as medicine to treat type II DM, but grape seeds are also expected to control blood sugar levels because the flavonoid content of the seeds also comes from the plant itself. It is hoped that grape seeds can overcome type II DM as effectively as grapefruit and leaves (Rahman et al., 2022).

Previous research has identified the prevalence of diabetes globally, specifically focusing on diabetes, as a significant public health concern (Ting et al., 2016). Diabetes has a serious impact on the organs of the body and can cause damage to the heart, kidneys, eyes, and nervous system (Jwad & AL-Fatlawi, 2022). At the national level, Indonesia has a high incidence rate of diabetes, with Indonesia ranked sixth in the world with the number of diabetes cases reaching 10.3 million in 2019.

Although previous studies have revealed antidiabetic potential in other parts of the vine, such as leaves and fruit, research on grape seeds has been less exploratory. This gap drives the need for more in-depth research to understand the extent to which grape seeds can be an effective solution to diabetes.

This study aims to critically evaluate the extent to which grape seed extract can effectively address diabetes symptoms in male white rats of the Wistar strain, provide deeper insight into its inner workings and potential as an antidiabetic drug, and is expected to contribute to the development of antidiabetic therapies and provide scientific evidence that can support the use of grape seed extract in clinical applications in humans.

METHOD

This research uses a true experimental design using the Pre-Post Test Control Group Design method. The population used _ in the study is a mouse white strain wistar, And the sample is a mouse white male, two months old. The subject study will be shared into five groups, including control positive (Subject given alloxan and drug antidiabetic), control negative (Subject given alloxan and distilled water), three groups of samples, respectively given alloxan And extract seed wine purple the dose consists from 75 mg/200gram BW, 125 mg/200gram BW, and 250 mg/200gram BW and given orally.

RESULTS AND DISCUSSION

The results of blood sugar levels in all treatment groups, both before being given alloxan and on the 14th day, have been compiled in the form of the following table.

Table 1 Data on Rat Blood Sugar Levels Control and Sample Groups

No	Group		Blood Sugar Levels (mg/dL)	Blood Sugar Levels 1 Day After Alloxan Administration (mg/dL)	7th Day Blood Sugar Levels (mg/dL), 2 Hours After Treatment	Blood Sugar Levels on Day 14 (mg/dL), 2 Hours After Treatment	A 7th Day Blood Sugar Level (mg/dL)	A 14th Day Blood Sugar Level (mg/dL)
1.	Positive Control (Metformin)	Rat 1	96	536	600	524	-136	12
		Rat 2	83	302	502	519	-200	-217
		Rat 3	64	185	104	103	81	82
		Rat 4	72	366	552	121	-186	245
		Rat 5	89	224	408	588	-184	-364
2.	Negative Control (Aquade's)	Rat 1	86	361	83	117	278	244
		Rat 2	77	520	600	600	-80	-80
		Rat 3	91	229	118	134	111	95
		Rat 4	84	416	481	571	-65	-155

No	Group		Blood Sugar Levels (mg/dL)	Blood Sugar Levels 1 Day After Alloxan Administration (mg/dL)	7th Day Blood Sugar Levels (mg/dL), 2 Hours After Treatment	Blood Sugar Levels on Day 14 (mg/dL), 2 Hours After Treatment	A 7th Day Blood Sugar Level (mg/dL)	A 14th Day Blood Sugar Level (mg/dL)
		Rat 5	71	341	255	600	86	-259
3.	Sample 1 (Extract Grape Seeds with a dose of 75 mg)	Rat 1	87	268	176	71	92	197
		Rat 2	94	366	95	56	271	310
		Rat 3	82	307	119	63	188	244
		Rat 4	74	452	82	439	370	13
		Rat 5	98	306	93	91	213	215
4.	Sample 2 (Extract Grape Seeds with a dose of 125 mg)	Rat 1	72	272	482	443	-210	-171
		Rat 2	76	315	55	235	260	80
		Rat 3	65	261	94	58	122	203
		Rat 4	91	277	93	117	184	160
		Rat 5	84	304	83	87	221	217
5.	Sample 3 (Extract Grape Seeds with a dose of 250 mg)	Rat 1	79	357	95	53	262	304
		Rat 2	62	536	297	101	239	435
		Rat 3	93	427	452	571	-25	-144
		Rat 4	81	403	69	96	334	307
		Rat 5	74	371	96	107	275	264

Information: Δ Blood Sugar Levels = the difference in blood sugar levels after administering alloxan on the 7th or 14th day. (+) indicates Δ that blood sugar has decreased. (-) indicates Δ that blood sugar has increased.

Table 1explains explains the control group and samples that had blood sugar levels tested. The treatment group before the mice were given alloxan, and the results showed that the blood sugar levels in each group of mice were ≤ 100 mg/dL. This shows that all treatment groups, both the control group and the sample group, did not experience type II diabetes mellitus (Langerman et al., 2022).

Based on data on blood sugar levels after being given alloxan, the results showed that blood sugar levels in each group of mice were ≥ 100 mg/dL. This shows that all treatment groups, both the control group and the sample group, experienced hyperglycemia (Type II Diabetes Mellitus).

Based on data on blood sugar levels on the seventh day after being given alloxan. The results showed that blood sugar levels in each group of mice experienced changes (Cai et al., 2023). Some experienced a decrease, and some even experienced an increase even though they had been given treatment to reduce blood sugar levels (Deora & Venkatraman, 2022). In the positive control, four mice experienced an increase when their blood sugar levels were tested on the seventh day. Then, for sample III, four mice experienced a decrease in blood sugar levels after being tested for blood sugar levels on day seven and compared with blood sugar levels after the treatment group was given alloxan (Atiya et al., 2022).

This shows that during treatment, each treatment group experienced changes in blood sugar levels, especially in the grape seed extract solution. Because on day 7, most of the sample group experienced a decrease in blood sugar levels compared to those after being given alloxan. Based on data on blood sugar levels on the 14th day after being given alloxan . The results showed that blood sugar levels in each group of mice changed. When compared with the results of blood sugar levels on

day 7, the results of blood sugar levels on day 14 were much better. Sample Group 3 provided the effect of reducing high blood sugar levels. The negative control group did not have the effect of reducing blood sugar levels. However, it increased the blood sugar levels of mice in the negative control group (Daniell et al., 2023).

Based on the table 1, Δ blood sugar levels compare the difference in blood sugar levels. Moreover, the table explains that on the 14th day, it had a significant impact, namely that blood sugar levels experienced a significant decrease in blood sugar levels after being given alloxan to the group of mice. However, on the 7th day, the results were not much different on the 14th day.

The research began by drying the grape seeds before extraction. Grape seed samples are dried because if the grape seeds are still wet, the sample will grow fungus, which can cause the contents of the grape seeds to become unstable and also to avoid rotting that occurs in fungi. Samples that have been dried are ground using a blender. The purpose of grinding is to make it easier for the sample to dissolve in the solvent used in making grape seed extract and to obtain a higher yield than samples that are not ground (Da Porto et al., 2013). The samples were extracted using the maceration method for 3x24 hours, and maceration was carried out two times. Samples that have been macerated will be thickened using a rotary evaporator. After the water content in the sample begins to decrease, the sample is thickened using a water bath for thickening. The reason for moving the thickening process is that when the sample in the rotary evaporator starts to thicken, and the water content of the sample starts to decrease, the sample will be difficult to remove. The sample will be left in the round flask container used in the rotary evaporator. Samples that have been thickened are stored in an airtight and watertight room to prevent the samples from growing mold or other pathogens that affect the contents of the grape seed samples.

Based on the data in the table, it shows the blood sugar levels in the control group and sample group before being given alloxan. The results showed that the blood sugar levels of mice in all treatment groups, both control and sample groups, were ≤ 100 mg/dL. From this table, it can be explained that the mice in the control and sample groups were still in normal condition, and the mice had not experienced type II diabetes mellitus.

Based on the data in the table, it shows the blood sugar levels in the control group and sample group after being given alloxan. The results showed that blood sugar levels in the control and sample groups after being given alloxan were ≥ 100mg/dL. This can explain why both the control group and the control sample experienced diabetes mellitus II. This is reinforced by the mechanism of alloxan, which can damage cells contained in insulin, where insulin can control blood sugar in the body (Gargouri et al., 2016).

Based on the data in the table, it shows the blood sugar levels in the control group and sample group on the seventh day after being given alloxan. The results showed that blood sugar levels in the control group and sample group experienced changes when compared with blood sugar levels after administering alloxan. This is indicated by the increase in blood sugar levels in the positive and negative control groups. The reason blood sugar levels in the positive control group increased was that the dose of metformin in this study could not have an effect in reducing blood sugar levels in mice. The second reason is that each white rat has a different metabolism in receiving metformin solution into the white rat's digestive system, so there are mice whose blood sugar levels decrease. There are mice whose blood sugar levels increase. Most of the sample group experienced a decrease in blood sugar levels. For sample groups 1 to 3, blood sugar levels in these sample groups mostly experienced a decrease in blood sugar levels compared to sugar levels after administering alloxan with blood sugar levels on the 14th day. Among the three sample groups, those that had good effectiveness in lowering blood sugar levels were sample group 1 and sample group 3. This was because grape seed extract samples given orally to white mice could lower blood sugar levels in white

mice compared to those with lower blood sugar levels. High blood pressure decreased simultaneously with the extract treatment for 14 days. This is reinforced by grape seed extract containing flavonoids, which have a mechanism for stimulating insulin to release pancreatic beta cells and flow into the blood. Besides stimulating insulin, flavonoids can also improve or restore insulin sensitivity in cells (Chan et al., 2019). Sample group 2 showed good data regarding the ability of grape seed extract samples to lower blood sugar. However, some mice showed that during treatment, both on day seven and day 14, when blood sugar tests were carried out, they did not show a decrease in blood sugar levels.

Based on the data in the table, it shows the blood sugar levels in the treatment group, both the control group and the sample group, on the 14th day after being given alloxan. The results showed that blood sugar levels in the control group and sample group experienced changes when compared with blood sugar levels after administering alloxan. This is proven by the positive control group's blood sugar levels still increasing and the sample group experiencing a decrease in blood sugar levels. Among the three sample groups, those that had high effectiveness in reducing blood sugar levels on the 14th day were sample group 1 and sample group 3.

CONCLUSION

as an antidiabetic drug in Wistar strain white rats. It can be concluded that this research shows that grape seed extract is effective in lowering blood sugar levels in Wistar strain white rats. This is indicated by blood sugar levels on day seven and day 14, showing a decrease in blood sugar levels. The dose of grape seed extract that effectively reduces blood sugar levels is a dose of 75 mg/200 gramsBB (Sample I) and 250 mg/200 gramsBB (Sample III). This is shown in sample group I; the average blood sugar levels on days seven and 14 were 113 mg/dL and 144 mg/dL. Sample group II with average blood sugar levels on days seven and 14 were 161.4 mg/dL and 188 mg/dL. Sample group III average blood sugar levels on days seven and 14 were 201.8 mg/dL and 185.6 mg/dL. The three sample groups showed a good reduction in blood sugar levels compared to the positive and negative control groups.

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