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Original Article

Cersenlau Sugar (Cherry Kersen & Telang Ungu): A Potential Antidiabetic Agent for Pancreatic Beta-Cell Repair in Rats

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ABSTRACT

This study aimed to find out the antidiabetic effects of CERSENLAU Sugar (Cherry Kersen & Telang Ungu) on the histological of the pancreas of diabetic rats. Method: The type of research used is purely experimental with a pre-post test control group design. The subject of the study was a male white Wistar rat (Rattus Norvegicus) aged 2-3 months and weighing an average weight of between 150-200 grams. On this plan the subject was randomized and then divided into 2 groups that is normal control and treatment group consisting of 4 subgroups namely: 1. The group diabetes was given commercial sugar diabetes and 3 diabetes groups were given CERSENLAU Sugar with different levels (100 mg/kg Body Weight; 200 mg/ kg Body Weight; 400 mg/Kg Body Weight). Each group consisted of six test animals. The total number of test animals was 30. Kruskall Wallis test to determine the significant differences between the treatment group and the control group with a p-value < 0.05 selected as the degree of significance. Results: CERSENLAU Sugar (Cherry Kersen Telang Ungu) contains phenols (86.63 mg), flavonoids (48.72), vitamin C (45,76 mg/100 ml), sugar (1,11%), anthocyanin (1,64 mg/100ml) and fiber (1,51%). Based on the results of the observations of the histopathology preparation of the pancreatic rat and the analysis carried out, it was proved that the administration of Cersenlau affected the histopathology figure of the pancreas of rats induced by alloxan. But at doses of 200 mg/kg Body Weight and 400 mg/ kg Body Weight, the effect is not very good compared to the dose of 100 mg/kg Body Weight which has a better effect. Conclusion: CERSENLAU Sugar (Cherry Kersen & Telang Ungu) repairs damage to pancreatic beta cells in mice with diabetes mellitus and affects pancreatic tissue regeneration as seen from the level of damage to pancreatic beta cells in animal models of diabetes.

Keywords : *Cersenlau Sugar, Cherry Kersen, Telang Ungu, Histologist, Pancreas, Diabetes Mellitus*

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INTRODUCTION

Type 2 diabetes mellitus is a chronic disease characterized by hyperglycaemia which is the result of the occurrence of body resistance to the effects of insulin produced by pancreatic beta cells [1]. According to the International Diabetes Federation (IDF), the prevalence of diabetes mellitus in the world is 1.9% and has made it the seventh leading cause of death worldwide. It is estimated from the prevalence of 463 million people in the world suffering from diabetes in 2019 and by 2030 the number of people with DM is predicted to climb up to 578 million and an increase is expected to 700 million patients in 2045 [2]. According to Rikesdas 2018, the prevalence of diabetes mellitus based on medical diagnosis in the population aged ≥ 15 years showed a figure of 2.0% and the prevalence of diabetes mellitus based on medical diagnosis in the population of all ages shows 1.5% [3].

During this time, commercial sugar products for diabetics that circulate on the market only offer that the sugar contains zero calories without containing phytochemical compounds that are beneficial as antidiabetics. This research wants to develop sugar products that have multiple benefits besides as sweeteners also have therapeutic benefits. Due to their higher nutritional value and content of health-promoting compounds, natural sugars offer potential benefits that can potentially mitigate the negative effects of refined sugar. This suggests that promoting reduced or eliminated consumption of refined sugar in favor of natural options could contribute to healthier dietary choices [4].

Cherry kersen (Muntingia calabura L.) and telang ungu (Clitoria ternatea) are two plants that have long been known to have health benefits. Recent studies have shown that these two plants also have the potential as anti-diabetes sugar. Cherry kersen contains flavonoid antioxidants that can protect pancreatic beta cells from damage caused by oxidative stress [5]. Oxidative stress is one of the factors that contributes to the development of type 2 diabetes. In addition, cherry kersen can also increase the proliferation of pancreatic beta cells, thereby increasing insulin production [6]. Telang ungu also contains flavonoid antioxidants that can protect pancreatic beta cells from damage [7]. In addition, telang ungu can also lower blood sugar levels by increasing insulin sensitivity and reducing glucose production in the liver [8].

The hypoglycaemic effects of *telang ungu* flower extract have been proven through several studies [9]. An oral administration of telang ungu extract (400 mg/kg BW) to rats decreased the serum glucose and Hb glycosylation as well as increased serum insulin, liver and bone muscle glycogen [10]. The administration of methanol, ethyl acetate or chlorophore extracts of up to 300 mg/kg BW Rats showed hypoglycaemic activity in albino rats that was more effective than the diabetic medication glibenclamide (10mg/kg)[11]. Hypoglycemia mechanisms through increased serum insulin secretion, glycogen levels, and active components that inhibit the formation of advanced glycation end products (AGEs) [12]. Ethanol extract lowers sugar in the serum of diabetic mice by inhibiting the activity of the enzymes β-galactosidase and β-glucosidase but does not inhibit the activity of the β-d-fructokinase enzyme [13]. Based on the findings, the researchers wanted to see the diabetic potential of the active compound in both the cersenlau sugar ingredients, the cherry kersen fruit and the purple oak flower. This study aimed to find out the antidiabetic effects of cersenlau sugar on the histological picture of the pancreas of diabetic rats.

METHOD

The type of research used is purely experimental with a pre-post test control group design. The subject of the study was a male white wistar rat (Rattus Norvegicus) aged 2-3 months and weighing an average weight of between 150-200 grams. The subjects of this study were obtained from the laboratory of Universitas Udayana. On this plan the subject was randomized and then divided into 2 groups that is normal control and treatment group consisting of 4 subgroups namely: 1. The group diabetes was given commercial sugar diabetes and 3 diabetes groups were given cersenlau sugar with different levels (100 mg/kg Body Weight; 200 mg/ kg Body Weight; 400 mg/Kg Body Weight). Each group consisted of six test animals. The total number of test animals was 30.

Before the treatment, both groups tested rate of pancreatic beta cell damage. After a specified period of time, both the treatment and control groups re-checkled histologic pancreatic. After the pancreas is removed from the body of the mouse, the preparation of the pancreatic preparation is performed with the following steps: The organ wash is washed using NaCl 0.9%, the fixation stage with formalin solution 10%, the dehydration stage using alcohol 70%, 80%, 90% and 95%, the clearing stage using toluene 3 times, respectively for 1-2 hours, the infiltration stage of paraffin using pure paraffin I, pure parafin II and pure paraffine III, followed by the embedding process, the organ stage is inserted into the paraffin blocks, the sectioning stage, the cutting stage of organ block using a microtome. With a strain density of 6 microns, staging stage, using Albumin MAYER, stage of deparaffination, using xylol for 15 minutes, staining stage, immersed in alcohol 95%, 80%, 70%, 60%, 50%, 40%, 30%, aquades 10 seconds, after which hematoxicillin. Washed the flowing water, soaked back into alcohol 30%, 40%, 50%, 60%, 70% then eosine. Then

back to alcohol 70%, 80%, 95%, then xylol for 10 minutes, Canada balm and then cover glass.

The microscopic data obtained was data scoring the degree of pancreatic damage of male white rats. The subsequent analysis used the nonparametric Kruskall Wallis test to determine the significant differences between the treatment group and the control group with a p-value < 0.05 selected as the degree of significance. If there are significant differences, then a Mann-Whitney test is performed to see what the differences mean for each group.

RESULTS

The measurement of the active substances contained in cersenlau sugar was carried out at the Food Technology Laboratory of Universitas Udayana. From the results of quantitative examination using the spectroscopic method, it was found that cerenlau sugar contains phenols (86.63 mg), flavonoids (48.72), vitamin C (45,76 mg/100 ml), sugar (1,11%), anthocyanin (1,64 mg/100ml) and fiber (1,51%).

Table 1. Bioactive Compound of CERSENLAU Sugar (*Cherry Kersen Telang Ungu*)

Test Parameters	Unit	Result
Total Fenol	mg GAE/ 100 mL	86,63
Total Flavonoid	mg QE/ 100 mL	48,72
Antioxidant Capacity	mg GAEAC/ 100 mL	178,25
Vitamin C	mg/ 100 mL	45,76
Beta carotene	mg/ 100 mL	ttd
Anthocyanin	mg/ 100 mL	1,64
Fiber	%	1,51
Total Sugar	%	1,11

The weight of the mice was weighed once a week to monitor the state of health of the rats and to know the progress of the weight of each week. The average weight development of mice of each group during the treatment is shown in Figure 1.

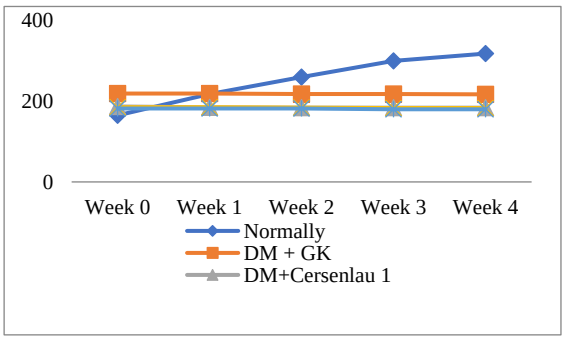


Figure 1. The average weight development of mice of each group during the treatment.

In the normal control group, there was an increase in weight from 171, 21 grams at the beginning of treatment to 323,02 grams on the end of treatment. In the diabetic group with commercial sugar, the weight at the start of treatment 214,53 grams decreased to 213, 22 grams in the end. The diabetes group treated with cersenlau sugar level 1 (100 mg/kg Body Weight) had a decrease in weight of 184, 13 grams to 180,47 grams after treatment.

The normal control group of rats experienced significant weight gain (p=0,000) during the treatment. The non-treated group of diabetic mice had an insignificant weight loss (p = 0,456). The group of diabetes mice with cersenlau sugar treatment had a significant decrease of 1.2, and 3 levels (p<0,005). Anova analysis showed that the average weight change in the group of diabetic mice control with commercial DM sugar, diabetes mices with censenlau sugar therapy was significantly different from the normal control (p < 0,005).

The microscopic data obtained was data scoring the degree of pancreatic damage of male white rats. Pancreatic beta cells in diabetic mice induced by alloxane showed damage. However, after treatment with Cersenlau sugar level 1 (100 mg/kg BW), level 2 (200 mg/ kg BW) and level 3 (400 mg/ Kg BW) improved at the end of treatment. Average changes in the damage score at the end of the treatment of each group can be seen in table 1.

Table 2. Rat Pancreatic Damage Score

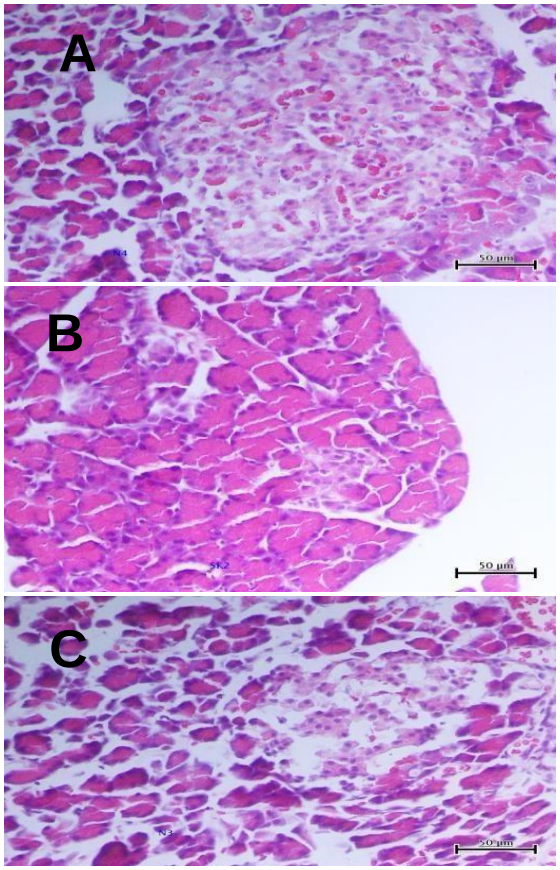
Groups	Damage Cell Score				Mean± SD Damage
	1	2	3	4	
Normally	0	0	0	0	4 ± 0^{c}
DM + GK	4	4	4	4	$1,25 \pm 0,5^{b}$
DM + GC 1	1	1	1	2	1.75 ± 0.5^{a}
DM + GC 2	2	2	2	2	2.25 ± 0.5^{a}
DM + GC 3	3	3	3	3	3 ± 0^{a}

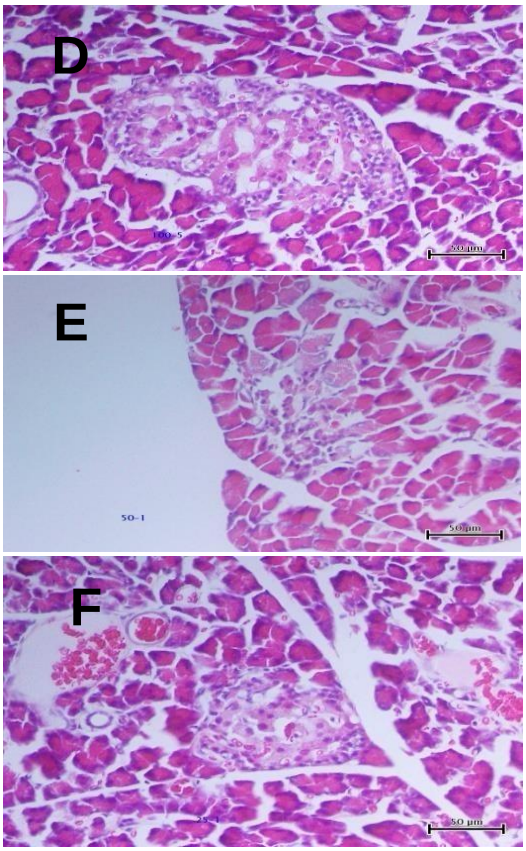
Based on the results of Mann-Whitney's analysis in Table 2 showed that there were significant differences in the histopathological picture of pancreatic mice from their respective treatment groups (p<0,05): the normal group differs significantly from all treatment groups, the DM control group with Commercial Sugar Diabetes is significantly different from the normal groups, and the 200 mg/kg BW dose control group (p <0,05), but differs non-

significantly from the 300 mg/ kg BW dose treatment group (p>0,05).

Based on the results of the observations of the histopathology preparation of the pancreatic rat and the analysis carried out, it was proved that the administration of Cersenlau affected the histopathology figure of the pancreas of rats induced by alloxan. But at doses of 200 mg/kg Body Weight and 400 mg/ kg Body Weight, the effect is not very good compared to the dose of 100 mg/kg Body Weight which has a better effect (Figure 2).

Based on data scoring pancreatic histological damage on the normal control given to Na CMC 0.5% obtained average rate of pancreas damage mice 0 seen no change, where the morphology of the island Langerhans still looks normal and the cells in it do not experience necrosis. On positive controls induced by alloxan and given CMC Na 0.5% as well as commercial sugar obtained averages of the rate of pancreatic damage of rats 4 suffered extremely severe cell necrosis. The occurrence of this necrosis is characterized by the presence of holes on the island of Langerhans. Necrosis is the death of cells or tissues as a result of a reversible degeneration process.





(A. Normally; B. DM + GK; C. DM + GC 1; D. DM + GC 2; E. DM + GC 3)

Figure 2. Histology of pancreatic tissue of mice with HE coloring with magnification 400x

DISCUSSION

Doses of 100 mg/ kg BW, doses 200 mg/kg BW and doses 400 mg/ Kg BW obtained average values of levels of pancreatic damage respectively (1,75), (2,75), and (3) showed a better figure of the morphology of the Langerhans island compared to commercial sugar DM control and relatively reduced necrosis cells. This suggests that the administration of cersenlau sugar can regenerate the beta cells of the pancreas. The diagram shows that commercial sugar DM controls experience the highest level of damage among all treatment groups.

Pancreas histological damage on normal control given Na CMC 0.5% obtained average rate of pancreatic damage mice 0 seen no change, where the morphology of the island langerhans still look normal and the cells in it do not experience necrosis. On negative control that is induced by streptozotocin and given

NaCMC 0.5% gained average value of the rate of pancreas damage 4 mice suffered very severe cell necrose. The occurrence of this necrosis is characterized by the presence of holes on the island of Langerhans. Living cells and tissues can succumb to necrosis, a process where they die due to irreversible damage. This can be triggered by various factors, such as poisonous substances, medication side effects, inadequate blood flow, extreme temperatures, radiation exposure, or physical injuries[14]. It shows that administering 0.5% Na CMC only functions as a suspending agent and has no regenerative activity on pancreatic β cells. On positive controls given commercial sugar obtained an average rate of pancreatic damage in the rat (1,25) the presence of necrosis in the Longerhans island cells was decreased. This is because metformin is a dimethyl derivative of mainly inhibits the formation of glucose in the liver as well as lowers LDL and triglyceride cholesterol and suppresses appetite and unlike sulphonylurea does not increase weight [15]. At doses of 100 mg/kg BW, doses 200 mg/ kg BW and doses 400mg/kg obtained mean values of pancreas damage rates (1,75), (2,75), and (3) respectively showed a better picture of the langerhans island morphology compared to negative control and relatively reduced necrosis cells. This suggests that the administration of Telang ungu cherry kersen sugar (cersenlau sugar) can regenerate the beta cells of the pancreas.

For decades, researchers have explored the use of antioxidant supplements to combat oxidative stress in type 2 diabetes [16]. These antioxidants are hypothesized to promote the proliferation and function of pancreatic β-cells, potentially improving overall disease management [17].

In mice with artificially induced high blood sugar (hyperglycemia) achieved through alloxan administration, an ethanol extract of cherry (Muntingia calabura L.) leaves significantly improved the histological structure of their pancreases, particularly the cells within the islets of Langerhans responsible for insulin production. Notably, the pancreatic structure of healthy mice was largely similar to those treated with a moderate dose of the extract (500 mg/kg body weight), suggesting the extract itself was not harmful to healthy pancreatic tissue [18].

Kersen leaves contain potent antioxidants, particularly flavonoids, which hold promise for alleviating type 2 diabetes. These antioxidants are believed to protect pancreatic beta cells within the islets of Langerhans, preventing damage and promoting their regeneration. This, in turn, could enhance insulin secretion, potentially offering therapeutic benefits for type 2 diabetic patients[19].

Administration of an ethanol extract of kersen leaves (Muntingia calabura L. folium) at an effective dose of 0.3 mg/g body weight significantly increased the number of pancreatic beta cells in white rats (Rattus norvegicus) of the Wistar strain previously induced with streptozotocin and nicotinamide (STZ-NA) to mimic type 2 diabetes[6].

In type 2 diabetes mellitus (T2DM), high blood sugar (hyperglycemia) triggers pancreatic beta cells to produce excessive reactive oxygen species (ROS) [20]. This rise in ROS leads to beta cell damage, ultimately impacting their quality and quantity. Various factors can influence the fate of beta cells in T2DM, including their ability to regenerate, survive, adapt to stress, resist cell death (apoptosis), and maintain proper metabolic function [21].

The regeneration of the pancreatic β cells occurs due to the presence of a compound contained in the purple of dandelions, one of which is a flavonoid, fenol, vitamin C and anthocyanin that plays a role in preventing damage to the beta cell in the pancreas by inhibiting the occurrence of oxidative stress.

CONCLUSION

CERSENLAU Sugar (*Cherry Kersen Telang Ungu*) repairs damage to pancreatic beta cells in mice with diabetes mellitus and has an effect on pancreatic tissue regeneration as seen from the level of damage to pancreatic beta cells in animal models of diabetes.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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