

THE EFFECT OF ALOIN ON BLOOD SUGAR LEVELS IN STREPTOZOTOCIN-INDUCED WHITE MALE MICE (MUS MUSCULUS)**Rendri Bayu Hansah¹, Dessy Abdullah², Thira Adiahni³****^{1,2,3}Universitas Baiturrahmah, Indonesia*****Correspondence Author: dessyabdullah@fk.unbrah.ac.id*****Abstract***

Blood, a lack of insulin secretion, insulin metabolism and both. One herb that works as well as drop in blood glucose levels and repair the metabolism of insulin is an aloin founded in aloe vera. Aims. Knowing the effect of aloin on white male mice (Mus musculus) induced by STZ. Methode. The type of research is experimental with the approach "pre-post test control group design". The population in the study is the white male (Mus musculus) 2-3 months, weighing 20-40 grams by 24 mice obtained from the university's pharmacological laboratory of Andalas. This sample was random with 24 mice. Data analysis shows the results of distribution are abnormal so the analysis tests used to friedman and the hoc wilcoxon post test. Results. The highest levels of blood glucose include K (+) 1, which is 273.5 mg/dL are affected by aloin for a drop in blood glucose in STZ (mus musculus), based on wilcoxon's test on K (+) 2 on metformin, P1 aloin dose 0.5 mg/kg, P2 dose 1 mg/kg has the same strength in drop in blood glucose level 0.028 and the most decline in pre-post value in P2 aloin group 1 mg/dL. Conclusion. There are effects of metformin administration, aloin dose 0.5 mg/kg and 1 mg/kg on lower blood glucose, aloin dose 0.5 mg/kg and aloin 1 mg/kg could be used as replacement therapy.

Key words: Aloin, Blood Sugar, STZ

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder that requires long-term medical care.(Care and Suppl, 2019) It is characterized by increasing glucose levels in the blood and metabolic disorders in the blood such as carbohydrates, fats, and proteins.(Fajrunni'mah, Lestari and Purwanti, 2017)(Rahmasari and Wahyuni, 2019) Diabetes results from a lack of insulin secretion, an insulin metabolism disorder as well as both.(Fajrunni'mah, Lestari and Purwanti, 2017) Diabetes mellitus type 2 (DMT2) is a hyperglycemia due to the lack of insulin in the cells' sensitivity to insulin produced by pancreatic cells. Insulin levels produced less or normal limits. The distinctive sign of DMT2, which is an increase in blood glucose due to insulin resistance and insulin secretion.(De Rosa et al., 2018)(Fatimah, 2015) More than 382 million individuals worldwide and is a leading cause of morbidity and mortality and Indonesia is the seventh of ten countries with diabetic by the International Diabetes Federation, with many cases occurred in developing countries. Some strategies, such as drug therapy are available to control it.(Kleinberger, Pollin and Medicine, 2016)(Kementrian kesehatan republik indonesia, 2020) For example, metformin is first line drug and anything drugs to but actually each drugs has own side effects especially for long-term administration.(Zhong et al., 2022) Therefore, discovery and

development of novel natural ingredients for treating DM with fewer adverse effects it will be the choice for society.

Streptozotocin (STZ) is a dm imaging drug through a nicotinadenine reduction in dinukleotida in the cells - pancreatic in the animal try. STZ synthesized by positive gram bacteria, *Streptomyces achromogenes* in antibacterial properties and is often used as a drug study for diabetic studies because of a specific toxicity linked to pancreatic cells. The effectiveness of STZ can be seen within 72 hours after delivery and depending on the dosage given The toxicity of the cells to STZ is due to protein carcinogens, DNA alkilation, free radicals (ros and RNS) and o-glcnase inhibitions. A dangerous incident after induction STZ was responsible for pancreatic tissue necrosis and in experimental dm in animal models. The mechanism of cellular malfunctions - pancreatic impairment by STZ in four ways, the others STZ was transported into a cell GLUT 2 through the GLUT 2 and there was DNA augmentation. Damage to DNA induces a polymerase, which leads to deplese (thinning) NAD + (cellular) and ATP to the death of pancreatic cells. The spontaneous release of oxidase nitrate by STZ, mitochondrial interference by NO , the ATP synthesis inhibition ultimately leads to cellular - corrosion death. Free radical formation such as superoxide (O₂), hydroxide (OH⁻), peroxide (ONOO⁻), causing cellular damage. The O-GlcNcase barrier by STZ, an irreverent formation of a glycooscillation protein that damages the cells - changing pancreas. (Busineni Jayasimha Goud, Dwarakanath.V, 2015).

Aloin is a slimy yellow fluid that lies between the flesh and the skin of the Aloe vera.(Septiani, Fatimah-muis and Anjani, 2020). Aloe vera contains 30% aloin, where there is aloin barbaloin and aloin isobarbaloin, inside is aloine, including aloin and resin (Marhaeni, 2020). One of the components of fenabolic compounds is aloine, which is also an antioxidant. Antioxidants can help lower the risk of dm type 2 and de-insulin resistance. In gill and sharma's 2014 research, it has proven the phenol and flavonoid compounds can counteract free radicals. Flavonoid has antioxidal activity that protects the body from reactive oxygen species (ros) damage that can prevent a degenerative disease. Flavonoid can be said to be antidiabetic because it can neutralize free radicals, thereby preventing damage to the insulin-producing pancreas (Sari, 2021).

MATERIALS AND METHODS

This research is an experimental study with pre-post test group design. Those experiment uses 24 mice divided for 4 group different treatments, positive control-1 given by STZ 45 mg/kgBB (K+ 1), positive control-2 given by STZ 45 mg/kgBB and metformin 1,3 mg/20 gr (K+ 2), treatment group-1 given by STZ 45 mg/kgBB and aloin dose 0,5 mg/kg (P 1), and treatment group-2 given by STZ 45 mg/kgBB and aloin dose 1 mg/kg (P 2). The criteria for including in animal testing include the following white male mice, 2-3 months and healthy. Hypperglicemia for mice is more than 175 mg/dL.

Make mice to hyperglycemia is use STZ dose 45 mg/kgBB on intraperitoneal, STZ dissolved NaCl pH 4,5 prepare with freash 10-15 minutes and injection it's only

once for DM. Before injection an animal, an animal adapted 1 week and fasted 12 hours.

The beginning of the experiment, mice glucose level must measure with gluco test, cutting tail 0,2-2 cm with surgical scissors, first drop of blood are removed and the second drops are touch on right stick glucose and it will be otomatic absorb, the result will be read on screen after 10 second and note the number on screen gluco-test. Observation of blood glucose are day 0 and day 3 after induced STZ, this situation obserb levels glucose. Normal blood sugar levels is 62-175 mg/dL, if levels glucose more than 175 mg/dL It's diabetic. Give the treatment in each group and chech glucose weekly for 1 month.

Extraction prepare, peeled of Aloe vera took lateks and meet, after than oven it on 650C temperature and up and down fire till dry up. It grind using grinder. Powder of Aloe vera in maseration with etanol 96% for 2 x 24 hours repetition. Filtrate maseration vaporized by rotary evaporator. The result filtration it suspend back with etanol and used for content analysis with HPLC.

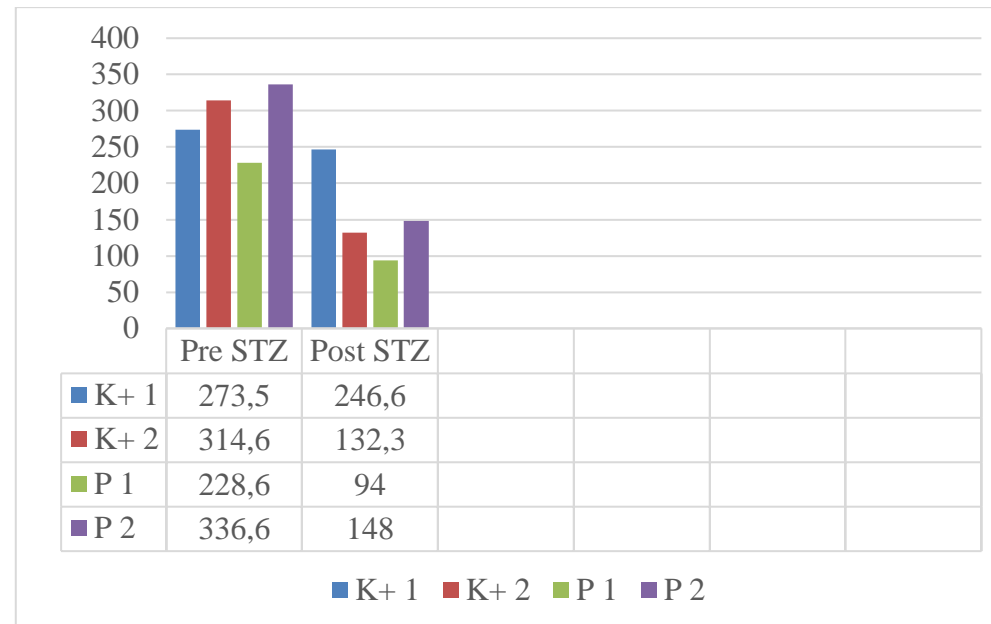
Testing slider chromatography, first, an extract of Aloe vera 100mg was diluted with a dichlorinated solvent and found a concentration of 10,000 ppm and the comparison of 10 milligrams was diluted with a dichlorometric suggestion found a concentration of 1,000 ppm. Taken 1 mL plus dichlorometan gets 100 ppm. Second, the construction of a motion phase consists of etil asetate 9 mL, n-hexana 9 mL, and asetat acid glacia 2 mL, wait until the saturated condition is, which is marked with the filter paper elimination already up to the top and wet. Third, the silent phase, a silica gel plate a size 100 x 50 mm made 2 testing points, for aloe vera extract as a sample and kuerteal as a comparison. Partial point 5 μ L samples and a comparison of 2 μ L. Fourth, the silica gel (silent phase) plate is inserted into the cember of the motion phase, lid and allow for the process of elimination to reach the upper boundary. when completed, a silent phase is retrieved and brandished out. Fifth, observe the blotches on silent phases under uv light 254 nm and 365 nm. Last, check spot stains, and rf count on each patch.

Analyze aloin with HPLC, First preparedness. Ten milligrams of cuertreat in pumpkin measuring 10 mL. More ethanol to the limit. Dissolve until all perfectly dissolved substances are obtained a solution mother of 1000 ppm. Run a thin series of 100, 75, 50, 50, 25, 10, 5, and 1 ppm, using bedsheets by UV 254 nm. Second, sample preparations. Give consideration to 50 mg of sample in a 10 mL flask, add ethanol to the boundary sign and mix to all dissolved substances (when sediment, filtered 0.2 m), and obtain a sample solution of 5000 ppm. Third, the silent phase of the shimadzu shim-pack McR-ods (6 mm x 250mm). fourth, A motion phase is 1 % acetic acid in H₂O and B motion phase is acetonitrile with flow rate 1 mL/minute. Fifth, testing is done with a standard solution test and extract into HPLC. HPLC results will show up on a peak pattern, showing an auc value on a standard rt. Sixth, calculating results using the calibration curve with $y = ax + b$ equation.

RESULTS AND DISCUSSIONS

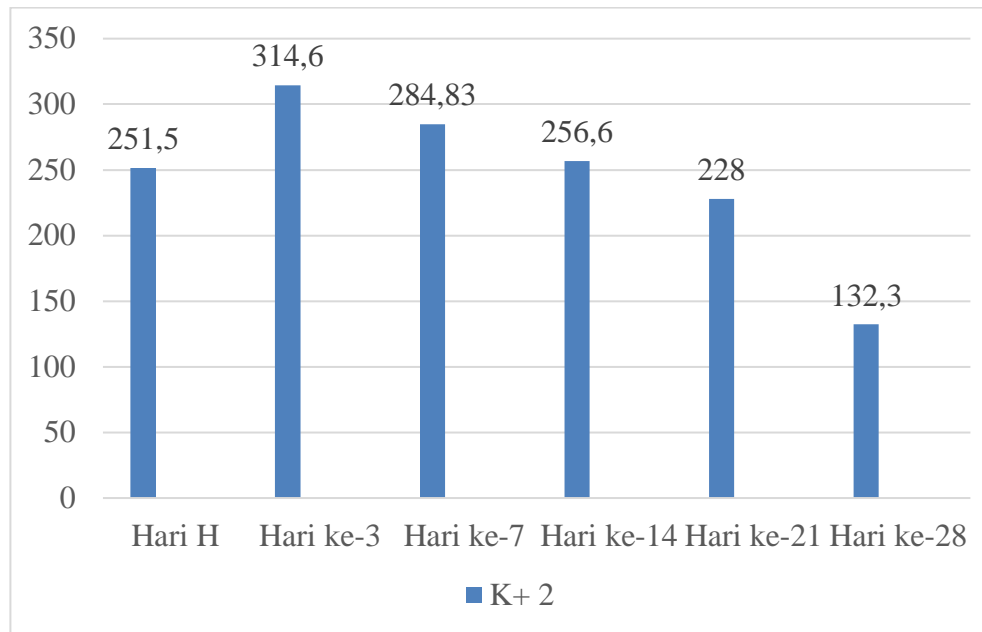
STZ effect to upper blood glucose levels

Streptozotocin (STZ) is a microbial cytotoxic agent to induce diabetes permanently. STZ was used as a cure for DM research because of its specific toxicity with pancreatic cells. STZ causes DNA alkylation and cellular necrosis irreversible. STZ is extremely soluble in water 50mg/dL, keton and low alcohol, and the maximum stability of STZ solution on pH 4 with stability falls on a higher or lower pH (Busineni Jayasimha Goud, Dwarakanath.V, 2015). Different STZ doses have a different process of making animal models hyperglycemia. A low-dose STZ results in a breakdown of pancreatic cells and triggers a process of inflammation that leads to loss of nerve activity, leading to insulin deficiency and hyperglycemia. This process is identical to dmt1 on patogenesis and the morphological changes. Single STZ high doses speed up diabetes, while induced STZ doses and a previous high diet will cause hyperglycemia with the approach of hyperinsulinemia and insulin resistance.(Furman, 2021).



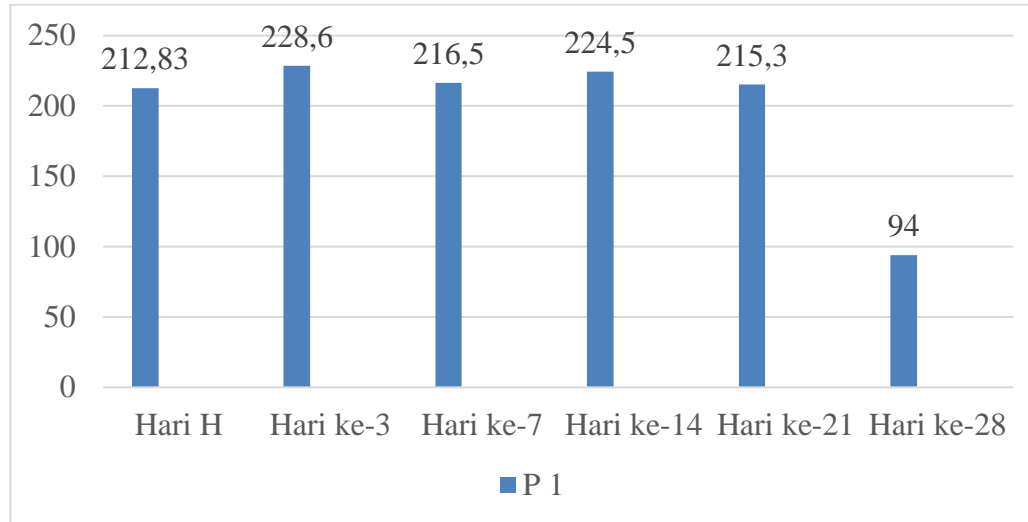
Metformin effect to reduce blood sugar levels

Metformin is a biguanide and is chosen as the first anti-diabetic oral drug. Metformin works by inhibiting the passage of the stomach, those maintaining greater hunger and weight loss. The mechanism works by increasing plasma levels of insulin and sensitivity through the glucose - line effect in the peripheral and also metformin, which inhibits the production of gluconeogenesis glucose. (Bintang Bella Pertiwi et al., 2021), (Amriani and Tuahatu, 2021).



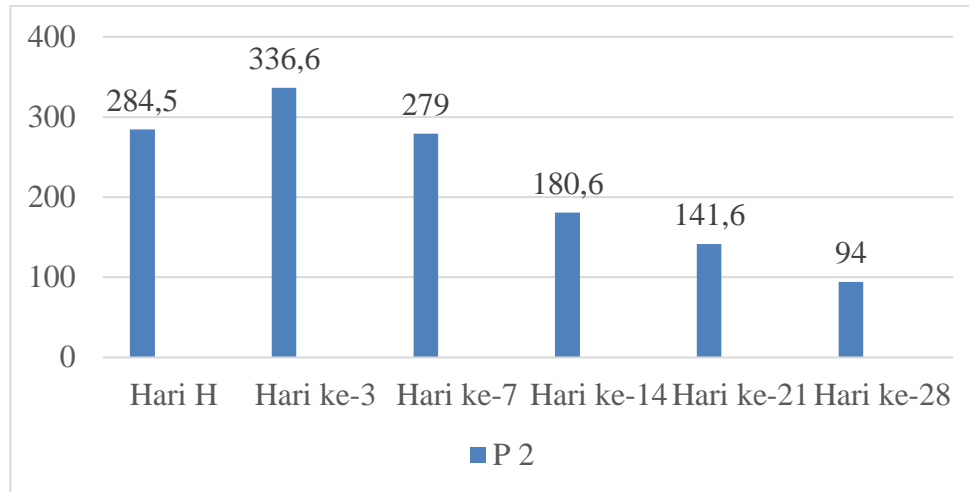
Aloin dose 0,5 mg/kg effect to reduce blood sugar levels

Dropper in blood glucose are due to the presence of antioxidant, flavonoid, and other properties of herbal plants especially Aloe vera. Ruting zong study 2022, animal treatment on glucose with a dose of aloin 40.78 mmol/L with 14 days time can have a better effect than normal groups. The study zhong ruting provides the basis for taking a dose of 0.5 mg/kg on this research (Zhong et al., 2022).



Aloin dose 1 mg/kg effect to reduce blood sugar levels

Research conducted by Ruting zhong in 2022 in aloin extract has hypoglycemic activity on the cells of IR-HepG2 in vitro and on the DMT2 in vivo mice which aloin has a antioxidant antioxidant behavior (Zhong et al., 2022). Antioxidants are compounds that can neutralize free radicals and therefore prevent degenerative diseases by binding free radicals and reactive molecules in the prevention of cell damage (Isdamayani and Panunggal, 2015). But in this study dose 750 µg/mL don't effect any inverted effects on the study.



Effects of a blood-sugar ratio with a dose of aloin 0.5 mg/kg and 1 mg/kg

Aloin doses 0.5 mg/kg and 1 mg/kg both have the effect of lowering blood glucose because aloin in the toxicity tests in HepG2 cells prove that alloys of up to 500 µg/mL doN't worsen the cell's integrity, while at higher doses of 750 µg/mL can reduce cellular life. An effect of aloin on glucose consumption in your IR-HepG2 cells is a metformin in a substantially reduced glucose consumption while in aloin with a dose 10-200 µg/mL relevant increases the glucose consumption to the catered HepG2 cell. An effect of aloin at dose 100 and 200 µg/mL suggests that aloin has a potential hypoglycememic effect comparable to metformin at 1.5µmol/L. Aloin can increase Hexsokinase enzymes (HK) and Piruvat Dehydrogenic (PDH) as the enzyme worth glycoyisis speed, hk increases glycogen of the liver and use glucose as an energy generator. Aloin on OGTT mice DMT2with 543.37 mmol/ l, 43.92 mmol/ l, and 40.78 mmol/ l have a better effect than normal groups.

CONCLUSIONS & RECOMMENDATIONS

STZ can make white male mice diabetic with low dose for 3 days and metformin, aloin dose 0,5 mg/kg and 1 mg/kg has the same power to kept blood sugar levels down for 1 month it's means aloin can be changed metformin for therapy diabetic herbal.

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