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The Effect Of Cholecalciferol On Fasting Blood Glucose In Streptozotocin-induced Hyperglycemia Mice

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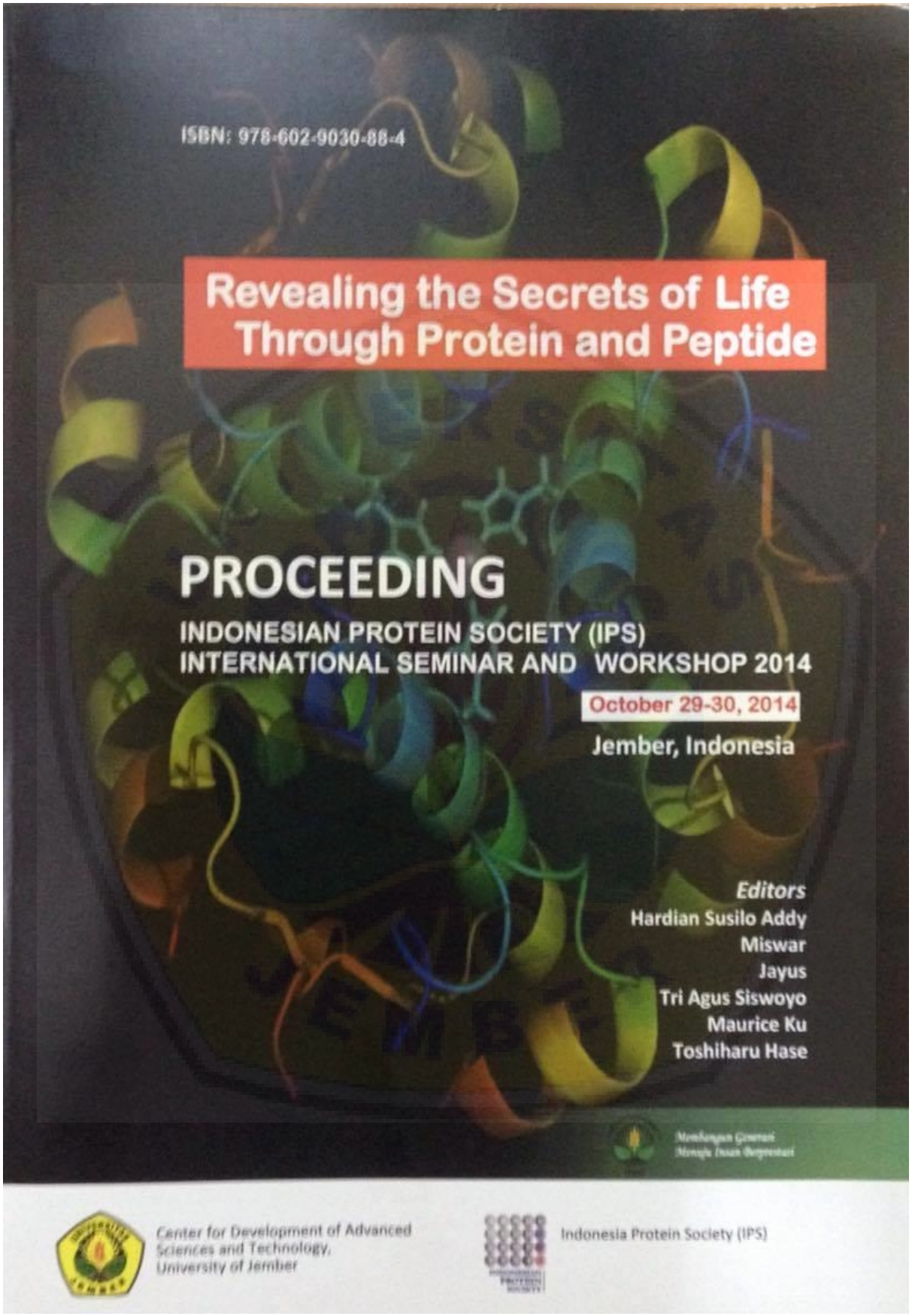

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Research Article

The Effect Of Cholecalciferol On Fasting Blood Glucose In Streptozotocin-induced Hyperglycemia Mice

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ABSTRACT

Glucose uptake into skeletal muscle cells require insulin-dependent and insulin independent signaling pathways, both leading to the translocation of glucose transporter-4 (GLUT4) to the plasma membrane. Insulin resistance occurs due to failure of insulin signaling to translocate GLUT4 resulting in the failure of glucose uptake and causing hyperglycemia. Cholecalciferol is known to have a function in regulating calcium homeostasis was shown to increase the synthesis of insulin and increasing insulin sensitivity. The purpose of this study is to explain the role of cholecalciferol to decreased fasting blood glucose in streptozotocin-induced hyperglyemia mice. 30 mice adapted for one week and then induced using 150mg/kgBW streptozotocin (STZ) intraperitoneally, After experiencing hyperglycemia mice were divided into 5 groups (n=6 each), Group I (hyperglycemic control), group II (25ng cholecalciferol), group III (50ng cholecalciferol), group IV (100ng cholecalciferol), and group V (metformin 300mg/kgBBB). Cholecalciferol given orally for 14th days. On day 15th the examination of fasting blood sugar levels were taken and the mice. Fasting blood sugar levels measured using a glucometer. Based on statistical analysis showed that there were significant differences in fasting blood sugar levels between treatment groups (p<0,001). Based on univariate regression analyses there was negative correlation of cholecalciferol with fasting blood glucose (p<0,001). Cholecalciferol may lower fasting blood sugar levels in hyperglycemia mice models.

Keywords : cholecalciferol, fasting blood glucose, STZ.

INTRODUCTON

Diabetes mellitus (DM) is a global health burden because the ever-increasing incidence, high mortality and morbidity and the economic impact in the treatment and prevention efforts is significant. DM patients has chronic hyperglycemia due to relative insulin deficiency and insulin resistance in target organs (muscle cells and adipose cells). In 2010 the prevalence of diabetes in the world were 6.4% (285 million people) and expected to increase to 7.7% (439 million people) in 2030. Indonesia ranks 9th (7 million cases) in 2010 and expected to increase to 6th (12 million cases) in 2030 (Shaw et al., 2010). The mechanism of insulin resistance is due to the failure of insulin signaling to translocate GLUT4 from intracellular to the muscle cell membrane. Resulting in the failure of glucose uptake which cause hyperglycemia. (De Fronzo, 2004). GLUT4 levels in diabetic patients is decreased approximately 90% due to the failure of insulin signaling, it is need to find an alternative path to translocate GLUT4 including by increasing calcium (Ca2 +) cytosol.

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Cholecalciferol is one form of vitamin D3. Cholecalciferol is known to have a function in regulating calcium homeostasis was shown to increase the synthesis of insulin by beta cells of the pancreas and increasing insulin sensitivity. Cholecalciferol can increase GLUT4 translocation through an alternative pathway that is independent of insulin is to increase calcium (Ca2+) cytosol (Chiu et al 2004, Martins et al 2007).

The aim of this study is to explain the role of cholecalciferol to decreased fasting blood glucose in streptozotocin-induced hyperglyemia mice.

MATERIAL AND METHOD

The 30 male mice (Mus-musculus) strain seis Webster (Balb/c) which had 25-30 gram body weight were used to this research. The mice were study placed on clean and quiet zone, the temperature of 270 C, 12 hours in lighting and 12 hours dark cycles, feded with pelet and drunk with distiled water. After adaptation, on first day the mice were injected STZ (Sigma Aldrich) single dose 150 mg/kgBB which disolved in citrate bufer 2,5 mg/ mL intrapertonealy. Mice were fasted in 4 hours to prevent aspiration and empty the stomach by not feding and sterilzation the cge from husk. On first night, after STZ injection, mice given dextrosa liquid 10% to avoid sudden hypoglycemic post injection. 2 days after that, mice were fasted in 6 hours and aspirated mice's blod from the tail to measure blod glucose used On Cal Plus Blod Glucose Monitoring System®. Induction be suces if blod glucose were 180-50 mg/dL (Etuk 2010).

After experiencing hyperglycemia mice were divided into 5 groups (n=6 each), Group I (hyperglycemic control), group II (25ng cholecalciferol), group III (50ng cholecalciferol), group IV (100ng cholecalciferol), and group V (metformin 300mg/kgBBB). Cholecalciferol (Sigma Aldrich) were given per oral in 14 days. In 15th day mice were fasted in 6 hours and aspirated mice's blod from the tail to measure blod glucose.

RESULT AND DISCUSSION

The result of STZ induction

Figure 1. Changes of Fasting Blood Glucose Levels after Administration of STZ

From figure 1 above was obtained that mice which given with 150 mg/kgBW injection intraperitoneal single dose had significant hyperglycemia on third day after STZ induction. The used of these dosage was alleged to have ocured Non Insulin Requirement (NIR) phases on the stage of the pathophysiology of diabetes in mice with reason that hyperglycemia control group can stay alive until day 14, and the treatment group with metformin may respond wel, even without insulin (Yamazaki et al 2009).

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Fasting blood glucose after cholecalciferol administration

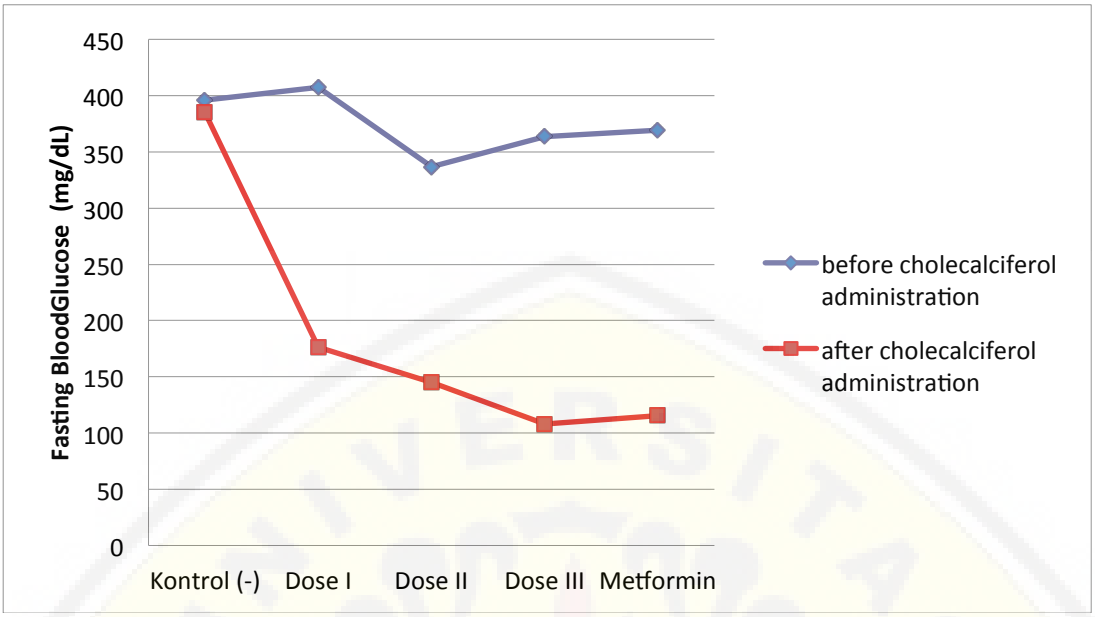

Figure 2. Fasting blood glucose before and after cholecalciferol administration

To determine the relation betwen the increase of cholecalcifereol with efect of the decrease of fasting blood glucose was on Figure 3.

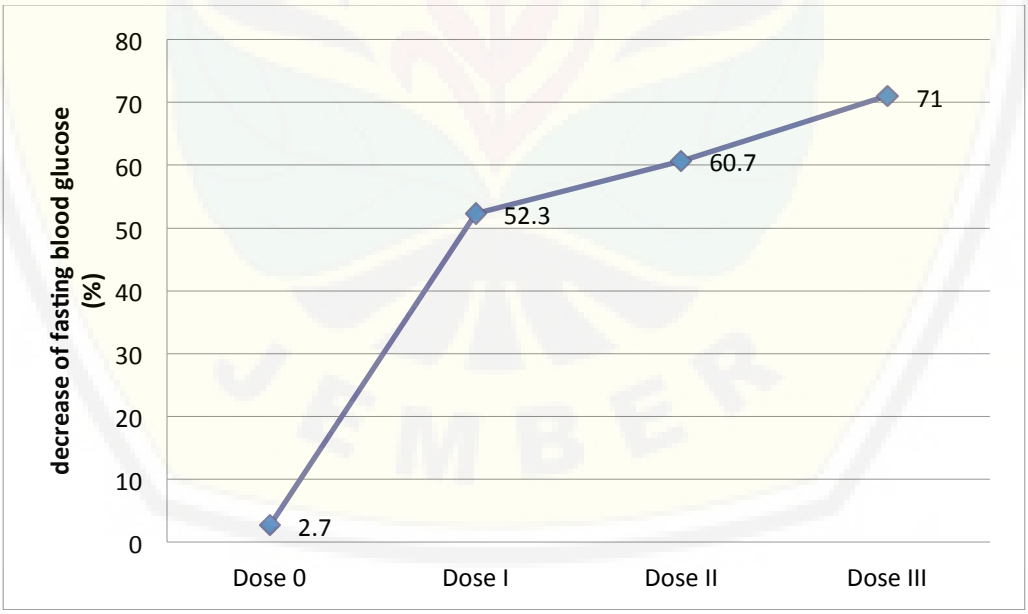

Figure 3. The relation of the percentage increase in dose of cholecalciferol with the decrease of fasting blood glucose.

Based on statistical analysis showed that there were significant differences in fasting blood sugar levels between treatment groups ($p<0,001$). Based on univariate regression analyses there was negative correlation of cholecalciferol with fasting blood glucose ($p<0,001$).

The administration of STZ caused DNA changes in pancreatic beta cels and DNA fragmentation via DNA alkylation. STZ was a NO donor in large doses, which it caused

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destruction of pancreatic beta cels and caused DNA damage. STZ also produced ROS that causes DNA fragmentation and cel damage. The bariers to synthesis and secrete insulin due to administration of STZ caused hyperglycemia in mice (Szkudelski 2001, Lenzen 2008).

Mechanism cholecalciferol alleged role in lowering blood glucose levels through a direct effect on insulin secretion choecalciferol. Cholecalciferol is inactivated by the enzyme 1-α-hydroxylase in pancreatic beta cells to its active form is 1,25(OH)2D3 which binds to its receptor in pancreatic beta cells. Further 1,25(OH)2D3 binds to vitamin D response element (VDRE) in the insulin gene promoter that activates transcription of the insulin gene so that the end result is increased insulin synthesis. Insulin secretion is a Ca2+-dependent process .Cholecalciferol to maintain the balance of intracellular Ca2+ is thus able to increase insulin secretion. Cholecalciferol also have receptors on skeletal muscle cells, cholecalciferol binding to its receptor produces genomic effects and non-genomic effects, which in turn will keep the balance of cytosolic Ca2+ to increase the stimulation of GLUT4 translocation to the cell membrane (Ceglia et al., 2012; Seshadri et al., 2011).

CONCLUSIONS

From this study it can be concluded that cholecalciferol may lower fasting blood sugar levels in hyperglycemia mice models.

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