Amerta Nutrition
e-ISSN: 2580-1163 (Online)
p-ISSN: 2580-9776 (Print)
Soviana et al. | Amerta Nutrition Vol. 9 Issue 3 (September 2025). 496-505

RESEARCH STUDY
English Version

OPEN ACCESS

The Effect of *β-Carotene* Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced *Streptozotocin-Nicotinamide*

Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide

Elida Soviana[1]*, Tea Aviarani[1], Puspito Arum[2,3]

[1]Department of Nutrition Science, Faculty of Health Sciences, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia
[2]Clinical Nutrition Study Program, Health Department, Politeknik Negeri Jember, Jember, Indonesia
[3]Graduate School of Medical Science, University of Groningen, Groningen, The Netherlands

ARTICLE INFO

Received: *04-11-2024*
Accepted: *28-05-2025*
Published online: *12-09-2025*

Correspondent:
Elida Soviana
elida.soviana@ums.ac.id

DOI:
10.20473/amnt.v9i3.2025.496-505

Available online at:
https://e-journal.unair.ac.id/AMNT

Keywords:
β-carotene, Nicotinamide, Streptozotocin, Triglyceride, Type 2 Diabetes Mellitus

ABSTRACT

Background: Hypertriglyceridemia is associated with decreasing insulin sensitivity and increasing insulin resistance in type 2 diabetes mellitus. *β-carotene* has a *cytoprotective* effect that can improve and protect β-cells of the pancreas, resulting in increased insulin synthesis and secretion.
Objectives: This research aimed to investigate the effect of *β-carotene* supplementation on triglyceride levels in high-fat diet and STZ-NA induced diabetes mellitus Wistar rats.
Methods: 18 Wistar rats were randomly divided into three groups: X_1 (negative controls), X_2 (positive controls), and X_3 (STZ-NA+*β-carotene* 10 mg/KgBW). High-fat diet intervention was given 14 days before diabetic induction in X_2 and X_3 groups. Wistar rats to be type 2 Diabetes Mellitus, received intraperitoneal injections of STZ 45 mg/KgBW and NA 110 mg/kgBW. Supplementation of *β-carotene* was given by the nasogastric feeding tube method every 2 days within 30 days. Triglyceride levels were measured using GPO-PAP. The effect of triglyceride levels after *β-carotene* supplementation was tested using a paired t-test and one-way ANOVA.
Results: Blood glucose levels in groups X_2 and X_3 increased by 188.34 g/dl and 186.34 g/dl after being injected with STZ and NA. There was a significant effect of triglyceride levels (p-value<0.001) after supplementation with *β-carotene* at a dose of 10 mg/kgBW. Triglyceride levels decreased by a mean of 21.90% or 28.42 mg/dl.
Conclusions: This research revealed that the supplementation of *β-carotene* at a dose of 10 mg/kgBW every 2 days within 30 days by the nasogastric feeding tube method can lower triglyceride levels in diabetic Wistar rats.

INTRODUCTION

Diabetes mellitus is one of the health problems with high mortality and morbidity rates in the world, including in Indonesia. Diabetes mellitus is a degenerative disease that is a silent killer, and most people do not realize they have diabetes mellitus until complications occur. Complications in diabetes mellitus include coronary heart disease, stroke, neuropathy, nephropathy, and retinopathy[1]. The International Diabetes Federation reported that in 2021, there were 537 million people, or 10.5% of the world's population (20-79 years old), suffering from diabetes mellitus. Indonesia has the sixth highest number after China, India, the USA, Brazil, and Mexico. By 2030, IDF estimates that 643 million people will suffer from diabetes mellitus, and by 2045, it will rise to 783 million. 90% of these cases are type 2 diabetes mellitus[2].

Type 2 diabetes mellitus is a glucose and lipid metabolism disorder due to impaired insulin secretion or insulin resistance. Insulin resistance is the failure of tissues to respond to the activity of the hormone insulin, but it is also a strong predictor of type 2 diabetes mellitus and hyperinsulinemia. In type 2 diabetes mellitus, there is increased formation of Reactive Oxygen Species (ROS), resulting in oxidative stress[3]. High levels of ROS can reduce total antioxidants. Research by Mohieldein et al

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

(2015) proved that prediabetic patients experienced increased oxidative stress characterized by decreased total antioxidants compared to healthy patients[4]. Antioxidants can protect the body from the negative effects of oxidants, free radicals, prevent inflammation by counteracting ROS, prevent the formation of ROS, and the occurrence of disease complications[3]. Oxidative stress in type 2 diabetes mellitus patients can also affect lipid metabolism by disrupting the function of enzymes involved in lipid metabolism, such as Lipoprotein Lipase (LPL) and hepatic lipase, which are important for regulating triglyceride levels in the blood. Decreased activity of lipid metabolism enzymes due to oxidative stress disrupts triglyceride breakdown and increases triglyceride levels in the blood. In addition, oxidative stress can also increase the production of Very Low-Density Lipoproteins (VLDL) by the liver, which is the main carrier of triglycerides in plasma. As a result, type 2 diabetes mellitus patients can experience hypertriglyceridemia[5].

Hypertriglyceridemia can be a risk factor that triggers the development of diabetes mellitus, can be a co-existing/concomitant condition, and can be a complication that can worsen glycemic control and increase the risk of cardiovascular disease and other complications. Early management and optimization of lipid control are key to minimizing its impact in patients with type 2 diabetes mellitus[6]. Elevated triglyceride levels are caused by excess glucose, which is converted into fatty acids and triglycerides mainly by fat tissue and the liver. Triglycerides formed in the liver are released into the plasma as triglyceride-rich VLDL, which will be stored in fat tissue, so in addition to glycemic control, diabetes mellitus patients also need to control blood lipids[5]. Patients with type 2 diabetes mellitus have severe insulin resistance and trigger gluconeogenesis so that basal glucose production by the liver increases[6]. Insulin resistance causes an increase in blood glucose levels and triggers the pancreas to produce more insulin so that blood insulin levels increase (hyperinsulinemia). Insulin resistance, especially in muscle, makes insulin lose its ability to stimulate glucose uptake in adipose tissue. It results in insulin no longer inhibiting the release of free fatty acids, increasing blood glucose and free fatty acid levels. The liver and kidneys try to maintain insulin sensitivity, and the resultant increase in insulin levels stimulates the liver to synthesize triglycerides. In conditions of hyperinsulinemia, there is an increase in free fatty acids (FFA) and a buildup of triglycerides in the liver. Serum levels of triglycerides and triglyceride-rich VLDL will increase due to increased triglyceride synthesis, as well as the synthesis and secretion of triglyceride-rich VLDL. Research by Selvi et al (2021), also shows an increase in triglyceride levels and high levels of HbA1c[7].

Triglyceride levels can be decreased by consuming antioxidants[8]. *β-Carotene* is one of the antioxidants with a cytoprotective effect that can repair and protect pancreatic β-cells, so insulin synthesis and secretion can increase[9]. Insulin activity in skeletal muscle, adipose, and liver cells increases, resulting in the absorption of excess blood glucose. *β-Carotene* in addition to being used as glycemic control can also be used as lipid control, especially triglycerides[10]. *β-carotene* supplementation plays a role in lipid control by preventing the acceleration of atherosclerosis formation in patients with diabetes mellitus by increasing bile acid secretion and reducing the concentration of cholesterol in plasma or liver cholesterol which will be used to regulate bile acids. The solubility and absorption of cholesterol can be inhibited by the presence of *β-carotene* by interfering with the formation of micelles in the small intestine[11]. Disruption of cholesterol synthesis will result in a decrease in VLDL chylomicron receptors that bind triglycerides in the liver and transport them to the blood and fatty tissues. The decrease in triglyceride binding occurs due to the reduction of VLDL chylomicron receptors, resulting in reduced triglycerides in the blood.

Ermawati et al (2014), proved that *β-carotene* supplementation through a round in experimental animals with a dose of 1 mg/kgBW, 10 mg/kgBW and 20 mg/kgBW for 30 days proved that the most efficient dose to reduce lipid profiles was a dose of *β-carotene* 10 mg/kg BW[12]. Wistar rats are one of the experimental animals often used in biomedical research in the laboratory. Rats were chosen because they have cell and organ functions that are biologically the same as humans. Rats commonly used for experimental research are male rats because they are not disturbed by hormonal influences. Wistar male rats are conditioned to DM by inducing *streptozotocin* (STZ) and *nicotinamide* (NA). *Streptozotocin* interferes with glucose oxidation, decreases insulin synthesis and secretion, and disrupts glucose transport and glucokinase activity in β-cells. *Nicotinamide* has a protective cytotoxic effect by inhibiting β-cytotoxins resulting from STZ injection. STZ-NA induced mice will experience hyperglycemia, which does not require external insulin injection to survive and experience glucose intolerance. STZ-NA induction can also increase triglyceride levels in plasma by 40% so that STZ-NA induction can condition rats into type 2 DM[13].

Based on this background, the purpose of this study is to investigate the effect of *β-carotene* administration at a dose of 10 mg/kg BW through a round 2 days once for 30 days on reducing triglyceride levels in Wistar Diabetes mellitus rats given high-fat feed and induced with STZ and NA. The benefit of this study is to provide information to the public about the effect of *β-carotene* on reducing triglyceride levels in patients with diabetes mellitus. This study can be used as a basis for utilizing food sources that contain *β-carotene* to lower triglyceride levels in the blood as a preventive measure against complications of Diabetes mellitus.

METHODS

This study was an experimental research trial laboratories in vivo on experimental animals with a randomized pre and post-test controlled group design. The rats used in this study were male rats Rattus Norvegicus Wistar strain, with a total sample size of 18 rats obtained from the Central Food and Nutrition Laboratory, Gadjah Mada University. The inclusion criteria include the age of 10-16 weeks, body weight 160-220 g, male gender, initial Fasting Blood Glucose (FBG) level <100 mg/dL, and post-induction FBG ≥126 mg /dL, with exclusion criteria if the post-induction FBG level of rats is <126 mg/dL. Examination of initial FBG levels with

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

the GOD-PAP method and initial body weight weighing using analytical digital scales was carried out on day 1 before the adaptation period. Subsequent weighing was carried out every week until the end of the study. This study consisted of 3 group designs: group X1 (negative control/normal), group X2 (positive control/STZ+NA), and group X_3 (treatment group/STZ+NA+ *β-Carotene* supplementation dose of 10 mg/kgBW).

Rats were kept in separate cages with a room temperature of 25–28 °C and a humidity level ranging from 70–75%. During the adaptation period and *β-Carotene* supplementation intervention, all groups were given Comfeed AD II standard feed and drink *ad libitum*. Groups X_2 and X_3, after the adaptation period on day 8, were given high-fat diet for 14 days. All maintenance procedures and research treatments have been adjusted to the ethical standards for experimental animal research. The research ethical code number is 2047/A.1/KEPK-FKUMS/IV/2019. The ethical approval was granted on April 4th, 2019, by the Health Research Ethics Commission, Faculty of Medicine, Universitas Muhammadiyah Surakarta.

Experimental animals were conditioned to develop type 2 diabetes mellitus by starting with high-fat feeding in groups X_2 and X_3 using standard Comfeed AD II feed supplemented with 1% cholesterol powder and 20% lard fat for 14 days, while group X_1 was given standard Comfeed AD II feed and *ad libitum* water. Then, the animals were induced with NA at a dose of 110 mg/kgBW dissolved in NaCl 0.9% and STZ at a dose of 45 mg/kgBW dissolved in citrate buffer 0.1M, pH 4.5, intraperitoneal single dose with at least 15 minutes interval between injections. Pre-treatment measurements of glucose levels using the Glucose Oxidase-Peroxidase Aminoantipyrine (GOD-PAP) method and triglyceride levels using the GPO-PAP method were performed 3 days after diabetic induction to ensure that the animals experienced developed hyperglycemia and increased blood triglycerides.

β-Carotene supplementation dissolved in 0.5% *sodium carboxymethyl cellulose* (NaCMC) suspension at a dose of 10 mg/kgBW was given to the X_3 group every 2 days for 30 days by mouth. During the intervention period, rats in all groups (X_1, X_2, and X_3) were given Comfeed AD II standard feed and *ad libitum* water. Post-test Triglyceride levels were measured 30 days after *β-Carotene* supplementation using the GPO-PAP method. Blood was taken through the retro-orbital plexus in a volume of 2 ml. Rats were fasted for 8-10 hours before blood collection to analyze triglyceride levels.

Statistical analysis using SPSS version 16 with a paired t-test to test the difference between pre- and post-treatment, with a significance p-value <0.05, which means there is a difference in triglyceride levels before and after treatment. To distinguish the effect after *β-Carotene* supplementation between groups, a one-way ANOVA test was used.

RESULTS AND DISCUSSIONS

Animal Characteristics Overview

A total of 18 male Wistar rats were included as subjects in this study, with their body weights were measured on a weekly basis from the initiation to the conclusion of the experimental period. The baseline measurement was recorded at the time of sampling, in accordance with the predefined inclusion criteria. Subsequent measurements were performed weekly, encompassing the adaptation phase, the two-week high-fat diet administration, the post-induction period following STZ and NA treatment, and the 30-day *β-carotene* supplementation phase. The average values and changes in body weight of the Wistar rats throughout the study are summarized in Table 1.

Table 1. Mean and Weight Change of *Wistar* Rats

Body Weight (g)	Group		
	X_1	X_2	X_3
Baseline[a]	178.17±3.06	172.83±5.56	176.83±2.64
Before Induction[b]	193.50±3.08	202.17±5.64	206.83±2.99
Pre-Treatment[c]	198.67±2.81	197.50±4.72	202.17±3.49
Post-Treatment[d]	230.00±2.61	179.17±5.42	231.17±3.19
Delta 1[e]	20.50	24.67	25.34
Delta 2[f]	5.17	-4.67	-4.66
Delta 3[g]	31.33	-18.33	29.00

X_1=negative/non-diabetic control group
X_2=positive/diabetic control group
X_3=STZ + NA + *β-Carotene* 10 mg/kgBW group
[a]) initial weight is the weight of the rats at the time of sampling based on the inclusion criteria
[b]) before induction is the weight of rats after the adaptation period, namely high-fat feeding for 14 days and before STZ-NA induction
[c]) pre-treatment is the weight of rats after STZ-NA induction and hyperglycemia had occurred
[d]) post-treatment is the weight of rats after STZ-NA induction and hyperglycemia and has received *β-Carotene* supplementation for 30 days
[e]) delta 1 is the difference between the baseline weight of the rats and their weight after receiving the high-fat diet for 14 days
[f]) delta 2 is the difference between the weight of rats before induction and after STZ-NA induction or before treatment
[g]) delta 3 is the difference between the BW of rats that have been induced by STZ-NA and after administration of *β-Carotene* for 30 days

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

Data on changes in the body weight of rats can be seen in Table 1. Based on Table 1, the initial body weight of the rats ranges from 172.83 g to 178.17 g, which shows that the initial body weight of the rats has met the research inclusion criteria. The body weight of Wistar male rats from the beginning of sample collection to the adaptation period and high-fat feeding, which spans 21 days, showed weight gain in the X_2 and X_3 groups, ranging between 24.67 g to 25.34 g. High-fat feeding contributes to weight gain in rats, because the high-fat feed given was the result of adding standard feed with cholesterol and fat powder[14].

The body weight of Wistar male rats induced by STZ 45 mg/kgBW and NA 110 mg/kgBW (after experiencing hyperglycemia) slightly decreased in the X_2 and X_3 groups, by 4.66 g to 4.67 g after 3 days of induction. The weight loss of rats is associated with the symptoms or general characteristics of hyperglycemia, namely polydipsia (drinking a lot), polyuria (excessive urine production), polyphagia (increased appetite), and sudden weight loss[6]. The main cause of weight loss in rats after being induced by STZ and NA is a result of lipolysis and gluconeogenesis. STZ and NA induction decreases the ability of pancreatic β-cells to synthesize and secrete insulin (insulin resistance), thereby reducing glucose absorption for energy metabolism. As a result, gluconeogenesis occurs, and fat and protein catabolism increases. The loss of tissue fat and protein results in a decrease in muscle mass and causes weight loss[15].

The X_3 treatment group, after receiving *β-Carotene* supplementation for 30 days, experienced an increase in body weight of 29 grams. Body weight in the X_3 treatment group given *β-Carotene* supplementation increased compared to that in the X_2 group (diabetic positive control group that was not given *β-Carotene* supplementation). *β-Carotene* has a cytoprotective effect that repairs and protects pancreatic β-cells, resulting in increased insulin synthesis and secretion[10]. Secreted insulin responds to high glucose levels in the blood and absorbs blood glucose into tissues, allowing glucose to be used for energy production and preventing gluconeogenesis[6]. The effect of *β-Carotene* in repairing and protecting pancreatic β-cells is what causes rats in treatment group X_3, given *β-Carotene* 10 mg/kgBW, to gain weight.

The positive control group experienced a continuous decrease until the end of the study, the weight loss reached 11.37%. Weight loss can occur becouse of type 2 diabetes mellitus as a result of STZ and NA induction in the positive control group rats. The induction of STZ and NA damages the β-cells of the pancreas, which can cause a decrease in insulin production, leading to an increase in glucose production by the liver while the transport of excess glucose into cells is reduced. This condition, where large amounts of glucose cannot be converted into energy, triggers gluconeogenesis, which causes a decrease in muscle mass and fat mass[6]. Rats in the negative control group (non-diabetic and without treatment) experienced an increase in body weight of 29.09%. Rats in the negative control group experienced a higher increase compared to the treatment group and the positive control group because the rats in the negative group were healthy or normal, resulting in a healthy appetite that supported weight gain.

Blood Glucose Levels

Streptozotocin and NA induction causes a decrease in pancreatic insulin synthesis and secretion, resulting in hyperglycemia. Examination of blood glucose levels is a parameter to determine if blood glucose has increased (hyperglycemia). Blood glucose levels of Wistar male rats in this study were checked twice: at the time of collecting the initial sample of the study to determine the sample according to the inclusion criteria of the study with fasting blood glucose levels <100 mg/dL, and 3 days after STZ and NA induction. Blood glucose levels were checked to ensure that the rats were diabetic before treatment. The complete blood glucose levels of Wistar male rats can be seen in Table 2.

Table 2. Mean and Changes in Blood Glucose Levels of *Wistar* Rats

Blood Glucose Level (mg/dL)	Group		
	X_1	X_2	X_3
Baseline[a]	70.45±2.91	72.63±4.06	72.73±3.20
Pre-test [b]	71.57±2.47	260.97±5.17	259.07±5.45
Delta[c]	1.12	188.34	186.34

X_1=negative/non-diabetic control group
X_2=positive/diabetic control group
X_3=STZ + NA + *β-Carotene* 10 mg/kgBW group
[a]) Initial is the blood glucose level taken at the beginning of taking samples of experimental animals according to the inclusion criteria
[b]) Pre-test is the blood glucose level of rats after STZ-NA induction and hyperglycemia
[c]) Delta is the difference between the initial blood glucose level and the pre-test

Based on Table 2, the mean blood glucose levels of Wistar male rats at baseline were between 70.45 mg/dL and 72.73 mg/dL. The mean initial fasting blood glucose levels showed that the Wistar male rat samples in all groups had met the research inclusion criteria of <100 mg/dL. Blood glucose levels in group X_1 (negative control/non-diabetic) increased from baseline to post-test by 2.13 mg/dL but remained within the normal range. The blood glucose levels of rats in the X_2 and X_3 groups increased after 3 days of STZ and NA induction, ranging from 186.34 mg/dL to 188.34 mg/dL (GDP≥126mg/dL), indicating that rats had developed hyperglycemia and entered type 2 diabetes mellitus.

Wistar male rats were conditioned for type 2 diabetes mellitus beginning with high-fat feeding for 14 days. The high-fat diet was given with the aim of making

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

rats experience metabolic syndrome, which initiates insulin resistance in Wistar male rats. High-fat feeding can be a factor in increasing blood glucose or causing hyperglycemia and hyperinsulinemia in experimental animals by causing decreased function of insulin receptors, inhibiting fatty acid oxidation in skeletal muscle, reducing messenger RNA (mRNA) activity and intracellular protein content of Glucose Transporter-4 (GLUT-4), and reducing GLUT-4 translocation to the cell membrane[16]. Fat feeding can also make rats develop metabolic syndrome and improve lipid profile.[17] The accumulation of free fatty acids in the liver can result in the production of Very Low Density Lipoprotein (VLDL) rich in triglycerides and high levels of triglycerides in the blood. The condition of high triglyceride levels in the blood triggers insulin resistance in patients with type 2 diabetes mellitus[18].

Research conducted by Marques et al (2016) proved that feeding high-fat food to two strains of rats, namely Wistar and Sprague-Dawley rats, for a long period of time is proven to make rats experience metabolic syndrome and experience a significant increase in blood glucose levels without induction. Research conducted by Wickramasinghe et al (2022) proved that feeding fat for 14 days and STZ induction in experimental animals, can make rats experience increased triglyceride levels and hyperglycemia[19]. Fat feeding in this study given for 2 weeks led to an increase in triglyceride levels, but the increase did not cause the rats to experience hypertriglyceridemia, or triglyceride levels exceeding 150 mg/dL. Fat feeding in this study was given to help improve the lipid profile, while to ensure that rats develop type 2 diabetes mellitus and experience increased triglyceride levels due to the effects of hyperglycemia, STZ and NA induction was required.

Streptozotocin is a type of antibiotic synthesized by *Streptomyces achromogenes* that has a selective toxic effect on pancreatic β-cells. *Streptozotocin* accumulates in the pancreatic β-cells by glucose transporter-2 (GLUT-2), which can cause damage to other surrounding organs such as the kidneys, liver and intestines. In β-cells STZ blocks glucose oxidation, decreases insulin synthesis and secretion and disrupts glucose transport and glucokinase activity. *Nitrosoamide* moiety of STZ through methyl carbonium causes methylation and DNA damage in pancreatic β-cells. Poly [ADP-ribose] Polymerase (PARP-1) activity in the pancreas causes ATP and NAD+ depletion, decreased protein synthesis and pancreatic β-cell necrosis. *Streptozotocin* in addition to DNA alkylation also causes β-cell death through oxidative stress and NO production, resulting in decreased insulin synthesis and secretion as well as impaired glucose transport and glucokinase activity leading to increased blood glucose levels or hyperglycemia[13].

Nicotinamide is niacin (Vitamin B3), which has antioxidant activity that can reduce the cytotoxic effects of STZ. Nicotinamide protects β-cells from STZ by inhibiting NO production, free radical generation, PARP activity, providing NAD +, inhibiting apoptosis through the prevention of *phosphatidylserine* and DNA degradation. These mechanisms allow STZ and NA-induced rats to develop type 2 diabetes mellitus due to the protective effect of NA against STZ. Rats induced with STZ and NA will experience hyperglycemia but do not require insulin injection to survive. *Streptozotocin* and NA induction not only causes hyperglycemia but also increases triglyceride levels by 40%[13]. Huamanchumo et al (2019) proved that a significant relationship between the incidence of hyperglycemia and increased triglyceride levels in type 2 diabetes mellitus[20]. This study used a dose of STZ 45 mg/kg/BW and NA 110 mg/kgBW, this dose can accelerate rats into type 2 diabetes mellitus within 72 hours or 3 days[13].

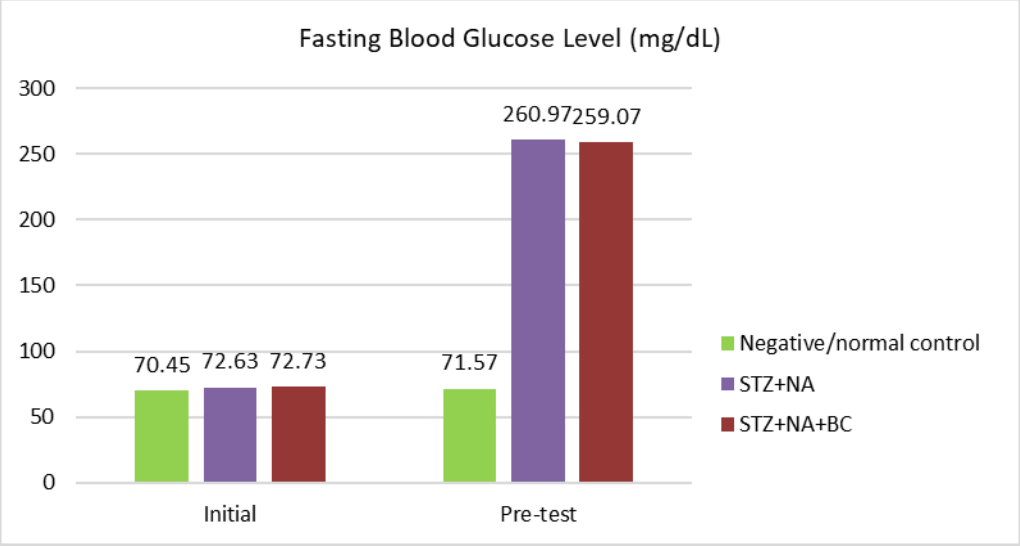

Figure 1. Blood Glucose Levels Before and After Treatment

Wistar male rats were subjected to an initial blood glucose examination to ensure that the experimental animals used as research samples were in accordance with the proposed inclusion criteria. The next examination was after 3 days of rats were induced with STZ and NA. The results showed that all samples, namely groups X_2 and X_3 induced by STZ 45 mg/KgBB and NA 110 mg/kgBW had developed hyperglycemia with fasting

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Jointly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

blood glucose levels ≥126 mg/dL, so the study could be continued with treatment in the form of *β-Carotene* supplementation at a dose of 10mg/kgBW, administered once every 2 days for 30 days to see its effect on reducing triglyceride levels. Changes in blood glucose levels in Wistar rats before and after treatment can be seen in Figure 1.

Triglyceride Level

Triglycerides are the most stored form of fat in the body, especially in adipose tissue. Fatty acids from excess triglycerides are stored as energy reserves in the form of fat in adipose tissue. Patients with type 2 diabetes mellitus experience insulin resistance, which triggers *gluconeogenesis*, leading to increased glucose production by the liver. This also affects muscle and fat tissue, causing the secretion of excess free fatty acids and resulting in increased blood triglyceride levels. Triglyceride levels of Wistar male rats in this study were influenced by dietary factors, which included high-fat feed given for 14 days after the adaptation period, in addition to the effects of insulin resistance from STZ and NA induction, which can increase triglyceride levels. The examination of triglyceride levels in this study was carried out twice: once after the rats were induced with STZ 45 mg/kgBW and NA 110 mg/kgBW (pre-test), and once after receiving *β-carotene* supplementation treatment at a dose of 10 mg/kgBW (post-test). The results of the triglyceride level examination can be seen in Table 3.

Table 3. Mean and Changes in Triglyceride Levels of *Wistar* Rats

Triglyceride Level (mg/dL)	Group		
	X_1	X_2	X_3
Pre Test[a]	77.31±2.95	136.31±5.86	129.42±5.32
Post Test[b]	80.95±3.48	137.97±6.10	101.00±2.45
Delta 1[c]	3.64	1.66	-28.42
p-value *1*[d]	0.005*	0.019*	0.001*

p-value 2[e]=0.001**

X_1=negative/non-diabetic control group

X_2=positive/diabetic control group

X_3=STZ + NA + *β-Carotene* 10 mg/kgBW group

[a]) Pre-test is the triglyceride level of rats after STZ-NA induction and hyperglycemia

[b]) Post-test is the triglyceride level of rats after STZ-NA induction and hyperglycemia and after *β-Carotene* supplementation for 30 days

[c]) Delta 1 is the difference between *pre-* and post-test triglyceride levels

[d]) *p-value 1 is the result of a paired t-test between pre-test and post-test rat triglyceride levels

[e]) **p-value 2 is the result of one-way ANOVA test between triglyceride levels of groups X_1, X_2, and X_3

Statistical analysis of triglyceride levels in groups X_1, X_2, and X_3 was conducted using a *paired t-test* since the data were normally distributed. This analysis aimed to determine the difference between pre-test and post-test in groups. The statistical test results showed that the X3 treatment group obtained a p-value of 0.001 at the 95% confidence level. Thus, it can be concluded that there is a significant difference between triglyceride levels before and after *β-carotene* supplementation at a dose of 10 mg/kgBW for 30 days. The negative control and positive control groups have p-value of 0.005 and 0.019 at the 95% confidence level, indicating a significant difference between pre- and post-test triglyceride levels.

Based on Table 3, the X_3 treatment group, there is a significant difference, as post-test triglyceride levels decreased by 21.90% or 28.42 mg/dL compared to the no treatment group X2, which increased by 1.2% or 1.6 mg/dL after 30 days of treatment. Statistical tests showed a significant difference in the non-treatment group, namely the X_1 and X_2 groups. However, the delta (the average difference) between the pre-test and post-test is very small and appears to increase when compared to the X3 treatment group, which showed a significant difference with a large decrease. The decrease in triglyceride levels can occur becouse of *β-carotene* supplementation at a dose of 10 mg/kgBW. This finding is in line with research conducted by Ermawati et al (2014), proved that the most efficient dose of *β-carotene* supplementation to reduce triglyceride levels is *β-carotene* is at a dose of 10mg/kgBW[12]. Triglyceride levels before and after treatment are shown in Figure 2.

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

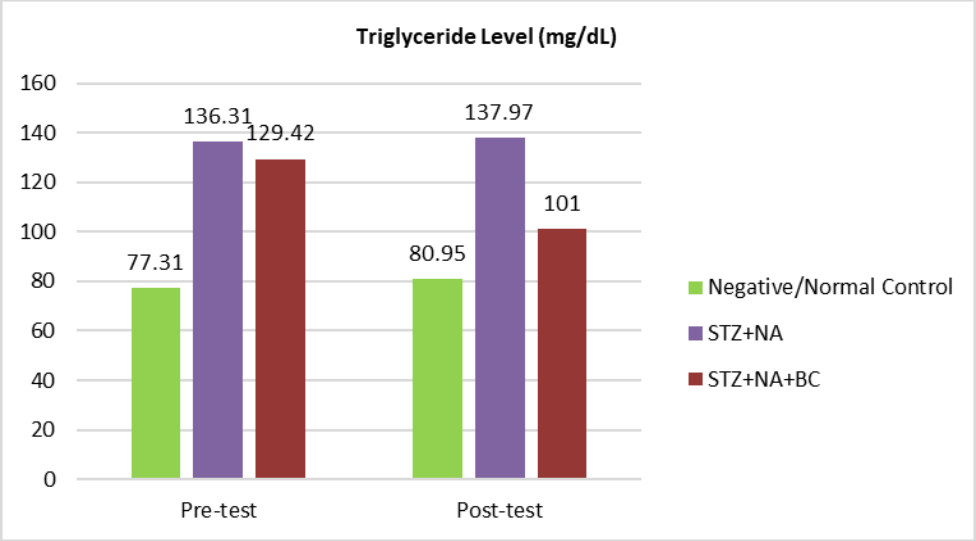

Figure 2. Triglyceride Levels (mg/dL) Before and After Treatment

Research by Navaro et al (2016) proved that the triglyceride-glucose Index (TyG Index) can be identified early in individuals who are at risk of suffering from type 2 diabetes mellitus. The relationship between triglycerides and insulin resistance is very close and centers on lipid and glucose metabolism disorders. High triglycerides in the blood occur due to excessive fat intake or metabolic disorders, which can cause fat accumulation in non-adipose tissue, such as muscle and liver. This accumulation triggers *lipotoxicity* that inhibits insulin signaling, especially in the pathways that regulate glucose uptake by cells. Additionally, high triglycerides are often associated with increased free fatty acid levels, which induce oxidative stress and chronic inflammation. This process exacerbates cellular dysfunction, reduces insulin sensitivity, and promotes insulin resistance[20]. Fatty acid accumulation that results in insulin resistance in skeletal muscle leads to an increase in the ratio between acetyl coenzyme A and coenzyme A and the ratio of NADH and NAD+ in the mitochondria, which triggers the inactivation of *pyruvate dehydrogenase*. Citrate concentration also increases, causing inhibition of phosphofructokinase and an increase in the intracellular concentration of *glucose-6-phosphate* (G6P). Increased G6P triggers glycogen synthesis and inhibits *hexokinase,* resulting in increased intracellular glucose concentration and decreased muscle glucose uptake[21].

An increase in intracellular fatty acids, such as *diacylglycerol* and acyl-CoA, activates serine/threonine kinase, which causes *serine/threonine phosphorylation* of insulin receptor substrates (IRS-1 and IRS-2). This phosphorylation reduces the ability of insulin receptors to activate *phosphatidylinositol-3-kinase* (PI-3-kinase), resulting in disruption of the insulin signaling pathway and insulin resistance. The free fatty acid accumulation mechanism that results in the weakening of IRS/PI 3 kinase signaling leads to a decrease in glucose transport by GLUT-4 into the cell membrane and the accumulation of excess glucose or hyperglycemia[21].

Hyperglycemia causes an increase in free radicals in patients with diabetes mellitus, which is also called oxidative stress. Oxidative stress in patients with diabetes mellitus can occur through three mechanisms: nonenzymatic *glycation* of proteins, *aldose reductase*, and *glucose autooxidation* during hyperglycemia, where free radicals can trigger damage to cell membranes. The danger of free radicals resulting from chemical reactions and metabolic processes, or oxidative metabolism that occurs in the body, can be overcome by antioxidants[22].

β-carotene is a provitamin A that functions as an antioxidant by suppressing oxidative stress. Food intake that lacks *liposoluble* antioxidants (*β-carotene*) can cause a lack of carotenoid concentration in the blood plasma, which can interfere with the ability of insulin to stimulate glucose in the muscle[9]. *β-carotene*, as an antioxidant, functions as a *peroxide radical chain* breaker by providing hydrogen ions to free radicals or by capturing singlet oxygen, thus inhibiting excessive free radical production. *β-carotene* as an antioxidant also plays a role in protecting the *hepatocyte* membrane of the HepG2 line by preventing free fatty acid peroxidation due to free radicals[23].

Research conducted by De Castro et al (2013) proved that there is an effect of *β-carotene* on the repair of STZ-induced pancreatic β-cells[16]. The *cytoprotective* effect of *β-Carotene* can repair and protect pancreatic β-cells, thereby enhancing insulin synthesis and secretion. As a result, insulin activity in skeletal muscle, adipose, and liver cells increases, resulting in the absorption of excess blood glucose. *β-Carotene* besides being used as glycemic control, can also be used as lipid control, especially triglycerides[10]. Research by Marcelino (2020) proved that by giving *β-Carotene* supplementation to diabetes mellitus rats that were induced by STZ and given additional 15% high-fat food for 14 days, there was a significant decrease in triglyceride levels[9].

β-carotene supplementation as lipid control plays a role in normalizing lipid oxidation and is important in preventing the accelerated formation of *atherosclerosis* in patients with diabetes mellitus by increasing bile acid secretion and reducing plasma or liver cholesterol concentration, which are used to regulate bile acids. The presence of *β-carotene* can also inhibit cholesterol solubility and absorption by interfering with micelles' formation in the small intestine. This disruption of cholesterol synthesis results in a decrease in chylomicron

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

and VLDL receptors that bind triglycerides in the liver and transport them to the blood and fatty tissues. Consequently, there is a decrease in triglyceride binding due to the reduction of chylomicron and VLDL receptors, resulting in decreased triglycerides in the blood[24].

Based on Table 3, the results of the one-way ANOVA statistical test indicate that changes in triglyceride levels show significant differences (p-value 0.001) between each group after receiving treatment. This indicates that *β-carotene* supplementation at a dose of 10 mg/kgBW can affect the decrease in triglyceride levels. Based on the one-way ANOVA test, it can be concluded that the administration of *β-carotene* at a dose of 10 mg/kgBW can significantly reduce triglyceride levels. The results in this study indicate that *β-carotene* has a significant effect on reducing triglyceride levels in Diabetes mellitus rats induced with STZ and NA. The results of this study are expected to influence the policy of *Perkumpulan Endrokrinologi Indonesia* (PERKENI) in the process of providing dietary treatment to patients with diabetes mellitus to consume food sources of *β-carotene. β-Carotene* at a dose of 10 mg/kgBW if converted to a human dose of 1.6 mg/kgBW. The application in humans with a weight of 50 kg is 80 mg *β-Carotene,* equivalent to *β-Carotene* in 1000 g carrots to be consumed every 2 days. Alternatively, diabetes mellitus patients can consume 850 g of boiled sweet potato every 2 days.

The primary strength of this study lies in its well-defined and rigorously controlled experimental design. Furthermore, the utilization of Wistar rats induced with STZ and NA offers a highly relevant and widely accepted model for type 2 diabetes mellitus. The study assessed key physiological parameters, notably blood glucose and triglyceride levels, which serve as valid and widely recognized indicators for evaluating the metabolic impact of *β-carotene*. Nevertheless, the study presents certain limitations, including a relatively short duration of intervention, limited to 30 days, which restricts the ability to evaluate the long-term metabolic effects of *β-carotene*. Moreover, the absence of supplementary data, such as histological analysis of pancreatic tissue or the evaluation of gene and protein expression, impedes a comprehensive understanding of potential β-cell regeneration mechanisms.

CONCLUSIONS

There is a significant effect of *β-Carotene* supplementation at a dose of 10 mg/kgBW given by sonde once every 2 days for 30 days on reducing triglyceride levels of Wistar Diabetes mellitus male rats given high-fat feed and induced with STZ and NA. This study shows that high-fat feeding can help increase the average triglyceride level to ±136 mg/dL, with the highest value of 144 mg/dL, while the cut-off point value of hypertriglyceridemia is >150 mg/dL. Furthermore, it is necessary to study how many days it takes for high-fat feeding so that blood triglyceride levels in Wistar male rats reach >150 mg/dL to ensure that rats given high-fat feed and induced by STZ and NA can also experience hypertriglyceridemia.

ACKNOWLEDGEMENT

Researchers would like to express their sincere gratitude to the Head of Laboratory Technician for the Center of Food and Nutrition Studies (PSPG), Universitas Gadjah Mada, for providing the necessary facilities for the maintenance of experimental animals, administration of treatment, and measurement of glucose and triglyceride levels. Appreciation is also extended to all team members who contributed to the successful completion of this study.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

All authors have no conflict of interest in this article. This research did not receive funding from sponsors or any party.

AUTHOR CONTRIBUTIONS

ES: conceived conceptualization, experimental design of the study, methodology, supervision, writing-review and editing; ES, TA: writing-original draft, data analysis, resources; PA: writing-review and editing, data analysis, resources.

REFERENCES

1. Cole, J.B & Florez, J.C. Genetics of Diabetes Mellitus and Diabetes Complications. *Nature Review Nephrology*. **16**, 377-390. (2020). https://doi.org/10.1038/s41581-020-0278-5
2. International Diabetes Federation (IDF). IDF Diabetes Atlas 10th Edition, International Diabetes Federation 2021. (2021). https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf
3. Ullah, A., Khan, A & Khan, I. Diabetes Mellitus and Oxidative Stress- A concise Review. *Elsevier. Saudi Pharmaceutical Journal*. **24**, 547-553. (2016). https://doi.org/10.1016/j.jsps.2015.03.013
4. Mohieldein, AH., Hasan, M., Al-Harbi, K.K., Alodailah, S.S, Azahrani, R.M & Al-Mushawwah, S.A. Dyslipidemia and Reduced Total Antioxidant Status in Young Adult Saudis with Prediabetes. *Diabetes Metab Syndr Clin Res Rev*. **9**, 287-91. (2015). https://doi.org/10.1016/j.dsx.2014.04.017
5. Hirano, T. Excess Triglycerides in Very Low-Density Lipoprotein (VLDL) Estimated from VLDL-Cholesterol could be a Useful Biomarker of Metabolic Dysfunction Associated with Stomatotic Liver Disease in Patients with Type 2 Diabetes. *J Atheroscler Thromb.* **31**, 1-12. (2024). https://doi.org/10.5551/jat.65164
6. Indonesian Endrokinology Society (PERKENI). *Guidelines for the Management and Prevention of Type 2 Diabetes Mellitus in Indonesia*. Jakarta: *PB PERKENI.* (2021). https://pbperkeni.or.id/wp-content/uploads/2021/11/22-10-21-Website-Pedoman-Pengelolaan-dan-Pencegahan-DMT2-Ebook.pdf

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

7. Selvi, N.M.K., Nandhini, S., Sakthivadivel, V., Lokesh, Shanmugam, Srinivasan, A.B & Sumathi, S. Association of Triglyceride-Glucose Index (TyG index) with HbA1c and Insulin Resistance in Type 2 Diabetes Mellitus. *MEDICA a Journal of Clinical Medicine.* **16**, 375-381. (2021). https://doi: 10.26574/maedica.2021.16.3.375
8. Forno, A.H.D., Camara, D., Parise, B., Rodrigues, C.F., Soares, J.J., Wagner, R., Ribeiro, S.R., Folmer, V., Puntel, R., Haas, S.E., Farias, F.M., Denardin, E.L.G., Denardin, C.C & Avila, D.S. Antioxidant and Lipid Lowering Effect of Dried fruits oil extract of Pterodon Emarginatusin Caenorhabditis elegans. *Arabian Journal of Chemistry*, 1-11 (2016). https://doi.org/10.1016/j.arabjc.2016.04.001
9. Marcelino, G., Machate, D.J., Freitas, K.D.C., Hiane, P.A., Maldonade, I.R., Pott, A., Asato, M.A., Candido, C.J., & Gumairaes, R.C.A. Beta Carotene: Preventive Role for Type 2 Diabetes Mellitus and Obesity: A Review. *Molecules*. **25**, 5803. (2020). https://doi.org/10.3390/molecules25245803
10. Roohbakhsh, A., Kaarimi, G & Iranshahi, M. Carotenoids in the Treatment of Diabetes Mellitus and its Complications: A Mechanistic Review. *Elsevier Biomedicine and Pharmacotherapy*. 31-42 (2017). https://doi.org/10.1016/j.biopha.2017.04.057
11. Rajia, S., Yeasmin, M., Mostofa Kamal, A. H. M., & Khanam, K. Antidiabetic and Antihyperlipidemic Activity of β-carotene on Streptozotocin-induced Diabetic Rats. *Journal of Pharmaceutical Research International.* **32**, 36-44. (2022). https://doi.10.9734/jpri/2022/v34i627283.
12. Ermawati, D., Rachmawati, B & Nyoman S.W. Effects of β carotene supplementation on total cholesterol, triglycerides, and malondialdehyde in diabetic Sprague dawley rats. *Indonesian Journal of Nutrition.* **2,** 47-52. (2014). https://doi.org/10.14710/jgi.2.2.47-52
13. Ghasemi, A., Khalifi, S. & Jedi, S. Streptozotocin-Nicotinamide-Induced Rat Model of Type 2 Diabetes (Review*). Acta Physiologica Hungarica.* **101**, 408-420. (2014). https://doi.org/10.1556/APhysiol.101.2014.4.2
14. Eluehike, N & Onoagbe, I. Changes in Organ and Body Weight, Serum Amylase and Antidiabetic Effects of Tannins from Spondias Mombin on Streptozotocin-induced Diabetic Rats. *Sabinet African Journal.* **3**. (2018). https://hdl.handle.net/10520/EJC-13b8ee0f1f
15. Petchi, R.R., Vijaya, C & Parasuraman, S. Antidiabetic Activity of Polyherbal Formulation in Streptozotocin - Nicotinamide Induced Diabetic Wistar Rats. *Journal of Traditional and Complementary Medicine Elsevier*. **4**, 108-117. (2014). https://doi.org/10.4103/2225-4110.126174
16. De Castro, U.G.M., Dos Santos, R.A.S., Silva, M.E., De Lima, W.G., Campagnole-santos, M.J & Alzamora, A.C. Age-dependent Effect of High-Fructose and High-Fat Diets on Lipid Metabolism and Lipid Accumulation in Liver and Kidney of Rats. *Journal of Lipids in Health and Disease BioMed Central*. **12,** 1-11. (2013). https://doi.org/10.1186/1476-511X-12-136
17. Qi, Y & Wang, X. The Role of Gut Microbiota in High-Fat-Diet-Induced Diabetes: Lessons from Animal Models and Humans. *MDPI Journals*. **15**, 922. (2023). https://doi.org/10.3390/nu15040922
18. Wang, Y., Fang, Y & Vrablik, M. Homeostasis Model Assessment for Insulin Resistance Mediates the Positive Association of Triglycerides with Diabetes. *Diagnostics (Basel)*. **14,** 733. (2024). https://doi. 10.3390/diagnostics14070733.
19. Wickramasinghe, A.S.D., Attanayajem A.P & Kalansuriya, P. Biochemical Characterization of High Fat Diet Fed and Low Dose Streptozotocin Induced Diabetic Wistar Rat Model. *Journal of Pharmacological and Toxicological Methods.* **113**. (2022). https://doi.org/10.1016/j.vascn.2021.107144
20. Navarro, D.G., Sanchez, L.I., Pastrana, J.D., Fernandez, A.M., Martinez, J.A. Triglyceride-glucose index (TyG index) in Comparison with Fasting Plasma Glucose Improved Diabetes Prediction in Patients with Normal Fasting Glucose: The Vascular-Metabolic CUN Cohort. *Preventive Medicine*. **86,** 99-105. (2016). https://doi.org/10.1016/j.ypmed.2016.01.022
21. Tahapary, D.L., Prastishita, L.B., Fitri, N.A., Marcella, C., Wafa, S., Kurniawan, F., Rizka, A., Tarigan, T.J., Harbuwono, D.S., Purnamasari & D., Soewondo, P. Challenges in the Diagnosis of Insulin Resistance: Focusing on the ole of HOMA-IR and Triglyceride/ Glucose Index. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. **16,** 8. (2022). https://doi.org/10.1016/j.dsx.2022.102581Get rights and content
22. Kusbandari, A., & Susanti, H. Beta-Carotene Content and Free Radical Capture Activity against DPPH (1,1-diphenyl 2-picrylhydrazyl) of Cantaloupe Fruit Extract (Cucumis melo var. Cantalupensis L.) by UV-Visible Spectophotometry. *Journal of Pharmaceutical Science and Community*. **14,** 37-42. (2017). http://dx.doi.org/10.24071/jpsc.141562

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*

23. Salem, S.A. Effect of two Carotenoids (Lycopene and β carotene) Supplementation on Hyperlipidemia and Lipid Peroxidation in Experimental Albino Rats. *Journal of High Institute of Public Health*. **45,** 1-7. (2015). https://doi:10.21608/jhiph.2015.20262.

24. Qiu, Z., Chen, X., Geng, T., Wan, Z., Lu, Q., Li, L., Zhu, K., Zhang, X., Liu, Y., Lin, X., Chen, L., Shan, Z., Liu, L., Pan, Aliu, G. Associations of Serum Carotenoids with Risk of Cardiovascular Mortality Among Individuals with Type 2 Diabetes: Results From NHANES. *Diabetes Care.* **45**, 1453-1461. (2022). https://doi.org/10.2337/dc21-2371.

Copyright ©2025 Faculty of Public Health Universitas Airlangga
Open access under a CC BY – SA license | Joinly Published by IAGIKMI & Universitas Airlangga

How to cite: *Soviana, E., Aviarani, T., & Arum, P. (2025) The Effect of β-Carotene Supplementation on Triglyceride Levels Study on Type 2 Diabetes Mellitus Wistar Rats Fed High-Fat Diet and Induced Streptozotocin-Nicotinamide: Pengaruh Suplementasi β-Carotene terhadap Kadar Trigliserida Studi pada Tikus Wistar Diabetes Mellitus Tipe 2 yang Diberikan Pakan Tinggi Lemak dan Diinduksi Streptozotocin-Nicotinamide. Amerta Nutrition, 9(3), 496–505.*