BIOMEDIKA
ISSN: 2085-8345, E-ISSN: 2541-2582
Vol 17, No. 2 Agustus 2025
doi: 10.23917/biomedika.v17i2.3734

EFFECT OF INULIN EXTRACT FROM DAHLIA TUBER *(dahlia variabilis)* ON CORONARY ARTERY HISTOPATHOLOGY IN RATS WITH TYPE 2 DIABETES MELLITUS (DM)

Zikrilla Mayuli Hopi[1], Ismawati[1*], Saryono[2], Ilhami Romus[1], Veni Dayu Putri[3], Sri Yanti[4], Fitri Dyna[4]

AFFILIATIONS
1. Faculty of Medicine, Universitas Riau
2. Faculty of Mathematics dan Natural Sciences, Universitas Riau
3. Nursing Study Program, Stikes Payung Negeri
4. Nursing Profession Study Program, STIKes Payung Negeri

ABSTRACT

Atherosclerosis in diabetes mellitus (DM) patients is prevented by using inulin to increase glucose metabolism and reduce cholesterol synthesis. Therefore, this research aimed to analyze dahlia tuber inulin extract to determine the effect on coronary artery histopathology in type 2 DM rats. A total of 20 male Wistar rats were divided into five groups, namely negative control without treatment, DM, DM + 0.5 mg/gBW/day inulin extract, DM + 1 mg/gBW/day inulin extract, and DM + 1.5 mg/gBW/day inulin extract. Furthermore, DM induction was carried out by administering 60 mg/kgBB streptozotocin and 120 mg/kgBB nicotinamide. The results of coronary artery histopathology readings showed that the highest and lowest scores of atherosclerosis were in Groups II (0,91±0,17) and V (0,08±0,1), respectively. Data analysis using Kruskal Wallis test reported significant results ($p<0.05$), while Mann-Whitney test showed differences between control and DM, DM, and inulin groups (III, IV, V). In this context, the administration of dahlia tuber inulin extract to rats induced by Type 2 DM prevented atherosclerosis in histopathological image of coronary artery.

KEYWORDS:
Coronary Artery, dahlia tuber, histopathology, Inulin, Type 2 DM

CORRESPONDING AUTHOR:
Ismawati
ismawati75@yahoo.com

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder in Indonesia and the world. The American Diabetes Association classification of DM is divided into four, namely type 1 DM, type 2 DM, other types of DM, and gestational DM[1]. Type 2 DM accounts for 90% of all diabetes cases and occurs due to a reduced insulin response known as insulin resistance. This type of DM is often reported in people over 45 years of age. Currently, different cases have been found in children, teenagers, and young adults due to increased obesity and lack of physical activity[2].

In 2021, the International Diabetes Federation stated that 6.2% of the world population, with more than 476 million people from 90 countries, were DM patients[3]. According to Riset Kesehatan Dasar (Riskesdas) 2018, the prevalence of DM over 15 years was 2% and showed an increase compared to the 2013 results for residents over 15 years of 1.5%. In 2019, Indonesia was in 7th place in the country with the highest number of cases[4]. In Riau Province, health services for DM patients will be 83.4% in 2022[5].

Type 2 DM starts with insulin resistance and is followed by pancreatic beta-cell dysfunction. This

insulin resistance occurs because the target cells typically cannot respond to insulin. Failure to treat the condition leads to progressive damage to the beta cells of the pancreas, resulting in insulin deficiency and necessitating the use of exogenous type by patients [6].

The classic symptoms of DM are polyuria, polyphagia, polydipsia, rapid weight loss, tingling, numbness, cramps, drowsiness, and blurred vision. The Indonesian Endocrinology Association divides DM complications into acute and chronic categories. Acute complications in DM include hypoglycemia and hyperglycemia, where blood glucose levels are below and above average in type 1 DM patients, causing metabolic ketoacidosis [6]. Meanwhile, chronic complications are divided into macrovascular and microvascular complications. Macrovascular complications are blockages in the large blood vessels of the heart and brain, such as coronary heart disease.

Coronary heart disease is caused by atherosclerosis, leading to insufficient oxygen supply to the heart, reduced nutrient delivery, and impaired heart function [7]. Research conducted in Europe stated that the intima-media thickened in 37-70.5% of patients with type 2 DM [8]. The role of metabolic syndrome is considered a cause of cardiovascular complications in patients.

Inulin is a group of natural polysaccharides which are fructose polymers. These polysaccharides are found in several types of tuber, including dahlia. Inulin is also a low-calorie carbohydrate of 1.5 kcal/gram and 60-65% lower than the levels of digested hexoses, such as glucose, and fructose. Digestive enzymes do not digest inulin when passing through the mouth, stomach, and small intestine, hence the compound is suitable for consumption by DM patients [9]. In this research, inulin was used as a diet to increase the metabolism of glucose and reduce the risk of DM. This polymer modifies the intestinal microbiota and stimulates the production of short-chain fatty acids to influence the expression of several proteins, resulting in increased intestinal permeability and insulin sensitivity [10].

Previous research on rats with type 2 DM included the administration of black rice composite flour biscuits, dahlia tuber inulin, and mocaf flour. The results showed that the treatment had a significant effect on reducing blood glucose levels [11]. In addition, the administration of inulin to dahlia tuber and chicory plants had anti-diabetic effects[9]. Research regarding the effects of inulin on atherosclerosis reported that inulin could lower cholesterol levels by inhibiting fat emulsification [12].

Based on the description above, the effect of dahlia tuber inulin extract on coronary artery histopathology is analyzed as a complication of type 2 DM. Scientific research discussing the impact of dahlia tuber inulin on complications of type 2 DM is still minimal. Therefore, this research aimed to

analyze the effect of dahlia tuber inulin extract on coronary artery histopathology in male Rattus norvegicus strain Wistar type 2 DM.

METHODS

This research was a continuation of previous results relating to the use of inulin extract [13]. Dahlia tuber used were obtained from Bukittinggi, West Sumatra Province, Indonesia. The extraction started by heating 2500 g of fresh dahlia tuber, cleaned and finely sliced in 5000 ml of distilled water for 30 minutes at 80°–90°C. Subsequently, the solution was cooled to room temperature and filtered to obtain the filtrate and residue. The filtrate was added with ethanol in a 1:1 (v/v) ratio, cooled at 4°C for 18 hours, and centrifuged for 10 minutes at 9000 rpm to obtain a white precipitate of inulin. The white precipitate was dried at 60°C until dry to obtain yellowish-white inulin. A certificate of passing ethical review No: B/046/UN19.5.1.1.8/UEPKK/2023 was received from the Medical and Health Research Ethics Unit, Faculty of Medicine, Riau University. This experimental research with a post-test-only control group design was conducted at the Biochemistry Laboratory, Faculty of Medicine, Riau University, and the Anatomical Pathology Laboratory, Faculty of Medicine, Riau University. The research period and data collection were from July to November 2023. The male *Rattus norvegicus* strain Wistar used were between the age of 2-3 months and weighed 200-250 grams in good health. The independent, dependent, and controlled variables were inulin extract from dahlia tuber, histopathology of coronary artery, and male *Rattus norvegicus* strain Wistar, respectively. A total of 20 experimental animals were divided into negative control without treatment + food, positive control, given streptozotocin (STZ) + nicotinamide (NA) + food, treatment group, given STZ + NA + feed + inulin extract 0.5 mg/gBW/day, treatment group with STZ + NA + feed + inulin extract 1 mg/gBW/day, and treatment group with STZ + NA + feed + inulin extract 1 .5 mg/gBW/day. Rats were subjected to a 12-hour fasting phase, before receiving an intraperitoneal injection of streptozotocin (STZ) at a dose of 60 mg/kg body weight dissolved in a 0.1M citrate buffer with a pH of 4.5. Meanwhile, 15 minutes of nicotinamide **(**NA) was administered at a 120 mg/kg body weight dose.

Rat heart organ was removed after termination and the tissue was washed with NaCl before slides were made using HE stain. An anatomical pathologist evaluated the microscopic preparations under a light microscope with a magnification of 400x in nine fields of view, and the average was calculated. Atherosclerosis score was used as a parameter for assessing lesions with the following scoring [14], Score 0- normal blood vessel histology, Score 1- initiation stage with macrophages and foam cells, Score 2- progression stage with an accumulation of smooth muscle intracellular lipids,

and Score 3- complication stage has surface defects in the form of fissures, ulcers, hematomas, and thrombus. The data obtained had an abnormal distribution and was analyzed using the Kruskal-Wallis test to examine differences between groups.

RESULT AND DISCUSSION

The results of coronary artery histopathology readings showed the highest and lowest scores in Groups II (0,91±0,17) and V (0,08±0,1), respectively.

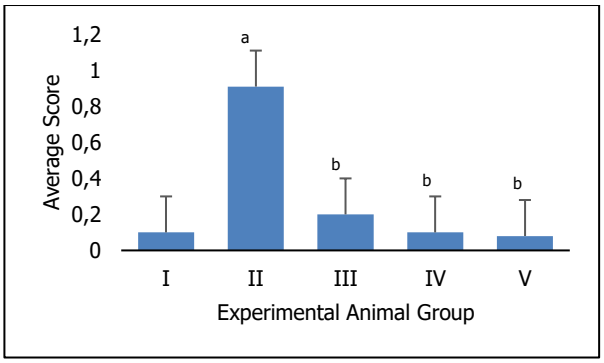

Figure 1. Average results of coronary artery atherosclerosis scores from each group of experimental animals. (a) Group II compared to I $p<0.05$, (b) Groups III, IV, and V compared to II have $p<0.05$ ($n=4$). Group I is a negative control rat without treatment, Group II is DM, Group III is DM + 0.5 mg/gBW/day inulin extract, Group IV is DM + 1 mg/gBW/day inulin extract, and Group V is DM + 1.5 mg/gBW/day inulin extract.

Significant results were obtained using the Kruskal-Wallis ($p<0.05$) and Mann-Whitney tests. A significant difference was found ($p<0.05$) between Groups I and II in Mann-Whitney test. Therefore, the induction administered could cause an increase in atherosclerosis lesion score. Groups II, III, IV, and V also found significant differences since the administration of dahlia tuber inulin extract reduced the formation of atherosclerotic lesions (Figure 2).

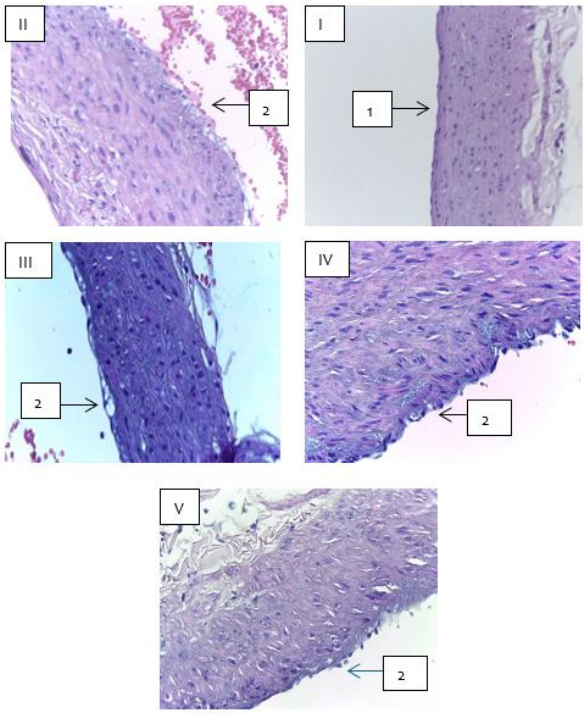

Figure 2. Histopathological images of coronary artery Groups I, II, III, IV, and V (HE staining) (1) intact endothelial cells (2) atherosclerotic foam cells. Group I is the negative control rat group without treatment; Group II is DM group; Group III is DM group + 0.5 mg/gBW/day inulin extract; Group IV is DM group + 1 mg/gBW/day inulin extract; and Group V is DM group + 1.5 mg/gBW/day inulin extract.

The results were in line with Monika (2017) on male Wistar *Rattus norvegicus* strains that gave a rice analog diet and streptozotocin induction. This led to an increase in foam cells in histopathological image of coronary artery compared to the control [15]. Another research conducted by Rijalun *et al.* (2021) on the same experimental animals induced by DM with STZ and NA showed an increase in atherosclerotic lesions in the thoracic aorta of DM group [16].

Dahlia is an ornamental plant that grows widely in Indonesia. Previous research reported that dahlia tuber contained 84.08% inulin [14]. In this research, three different doses of inulin were used, namely 0.5 mg/gBB/day, 1 mg/gBB/day, and 1.5

mg/gBB/day. These doses caused a significant difference by decreasing atherosclerosis lesion score. The results of histopathological readings of coronary artery of male *Rattus norvegicus* strain Wistar in DM group with an inulin dose of 0.5, 1, and 1.5 mg/gBW/day found an average of 0.22 ± 0.23, 0.11 ± 0.08, and 0.08 ± 0.10, respectively. Inulin 0.5 mg/gBW/day was reported as the lowest dose reducing atherosclerotic lesions in coronary artery.

According to Marie et al. (2006), dietary inulin from chicory roots significantly reduced atherosclerotic plaque in the aortic sinus compared to the control given a sucrose diet [17]. Dina *et al.* (2023) reported that a rice analog diet containing inulin from gembili tuber reduced triglyceride levels in rats with type 2 DM. A decrease in triglycerides led to an increase in high-density lipoprotein (HDL) and a reduction in low-density lipoprotein (LDL)[18]. This prevented the formation of atherosclerotic plaque concerning the ability of inulin to modulate intestinal microbiota. Different research showed that gut microbiota had an essential role in the occurrence of inflammation and metabolic disorders such as obesity, insulin resistance, and type 2 DM. Cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and high-sensitive C-reactive protein (hs-CRP) caused a series of inflammatory processes, insulin resistance, and β-cell dysfunction [19,20].

The administration of dahlia tuber inulin extract to type 2 DM rats prevented the formation of atherosclerotic lesions. However, this research has limitations since the mechanism of action of dahlia tuber inulin cannot be explained.

CONCLUSION AND SUGGESTION

In conclusion, dahlia tuber inulin extract prevented the formation of atherosclerotic lesions in coronary artery of rats with type 2 DM. Suggestions for further analysis included research regarding the mechanism of action of inulin in reducing oxidative stress on the formation of atherosclerotic lesions.

REFERENCES

1. Care D, Suppl SS. Classification and diagnosis of diabetes : standards of medical care in diabetes. Diabetes Care. 2022;45:17–38.
2. Pouwer F, Speight J. Diabetes mellitus, type 2. Camb Handb Psychol Health Med Third Ed. 2022;481–2.
3. international diabetes federation. International diabetes federation Atlas. Diabetes Res Clin Pract. 2021;10.
4. RI PD dan IKK. Kementrian Kesehatan RI. 2020. Infodatin diabetes melitus.
5. Riau DKP. Laporan kinerja instansi daerah provinsi riau tahun 2022. 2022.
6. Fatimah RN. Diabetes melitus tipe 2. J Major. 2015;4.
7. Pengaribuan JJ, Tedja C, Sentosa W. Perbandingan metode algoritma C4.5 dan extreme learning machine untuk mendiagnosis penyakit jantung koroner. Inform Eng Res Technol. 2019;1(1):1–7.
8. Tedjasaputra SE, Yunir E, Wijaya IP, Setiati S. Faktor-faktor determinan dan nilai tambah osteoprotegerin (OPG) dalam mendeteksi penebalan tunika intima-media (TIM) karotis pada pasien diabetes melitus tipe 2. J Penyakit Dalam Indones. 2018;5(2):63.
9. Sunarti S, Ginting CN, Ginting SF. Potensi inulin umbi dahlia sebagai anti diabetes. J Keperawatan Prior. 2022;5(1):53–65.

10. Miao M, Dai Y, Rui C, Fan Y, Wang X, Fan C, et al. Dietary supplementation of inulin alleviates metabolism disorders in gestational diabetes mellitus mice via RENT/AKT/IRS/GLUT4 pathway. Diabetol Metab Syndr. 2021;13(1):1–14.
11. Manullang B, Julianti E, Nainggolan RJ, Pangan T, Pertanian F, Medan U. Efektivitas biskuit tepung komposit beras hitam (Oryza sativa L.), inulin umbi bunga dahlia dan tepung mocaf terhadap kadar glukosa darah pada tikus (Rattus norvegicus) penderita diabetes melitus tipe II. J Food Life Sci. 2018;2:115–21.
12. Fairudz A, Nisa K. Pengaruh serat pangan terhadap kadar kolesterol penderita overweight. Med J Lampung Univ. 2015;4(8):121–6.
13. Putri VD, Yanti S, Dyna F, Saryono S, Ismawati I. The extraction and characterization of inulin from dahlia bulbs (Dahlia variabilis). AIP Conf Proc. 2022;2708(November).
14. Ismawati, Oenzil F, Yanwirasti, Yerizel E. Changes in expression of proteasome in rats at different stages of atherosclerosis. Anat Cell Biol. 2016;49(2):99–106.
15. Roosyidah M, Efendi E, Hairrudin. Pengaruh Pemberian Diet Beras Analog terhadap Gambaran Histopatologi Arteri Koroner Jantung Tikus DM Tipe 2. J Agromedicine Med Sci. 2017;3(3):44–9.
16. Arridho R, Ismawati I, Asni E, Romus I. Efek Pemberian Asam Alfa Lipoat pada Histopatologi Aorta Torakalis Tikus Diabetes Melitus Tipe 2. J Ilmu Kedokt J Med Sci. 2021;14(1):33.
17. Rault-Nania MH, Gueux E, Demougeot C, Demigné C, Rock E, Mazur A. Inulin attenuates atherosclerosis in apolipoprotein E-deficient mice. Br J Nutr. 2006;96(5):840–4.
18. Rosilawati DH. Pengaruh Pemberian Beras Analog Umbi Gembili (Dioscorea esculenta) Terhadap Kadar Trigliserida Pada Tikus Diabetes Melitus Tipe 2. 2023;15(2):1–10.
19. Deghan P, BP, MA J abadi, A.A. Inulin controls inflammation and metabolic endotexemia in women with type 2 diabetes mellitus : a randomized-controlled clinical trial. Int J Food Sci Nutr Int J Food Sci Nutr. 2014;65(117).
20. Colantonio AG, SL W, B.M. The effect of probiotics and substances with prebiotic properties on metabolic and inflammatory biomarkers in individuals with type 2 diabetes mellitus. J Acad Nutr Diet. 2020;120:587–607.