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EFFECT OF DAHLIA TUBER INULIN EXTRACT ON THE THICKNESS OF THE THORACIC AORTIC TUNICA INTIMA-MEDIA IN TYPE 2 DIABETIC RATS MODEL

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ABSTRACT

Inulin is a natural polysaccharide that improves glucose metabolism and reduces cholesterol levels through the formation of short-chain fatty acids, which may contribute to preventing atherosclerosis in type 2 diabetes mellitus (T2DM). Therefore, this study aimed to evaluate the effect of dahlia tuber inulin extract on the thickness of the thoracic aortic tunica intima-media (TIM) in T2DM-induced rats. A total of 20 male Wistar rats were divided into five groups: control, T2DM, T2DM + 0.5 mg/gBW/day inulin extract, T2DM + 1.0 mg/gBW/day inulin extract, and T2DM + 1.5 mg/gBW/day inulin extract. T2DM induction was performed using 60 mg/kgBW streptozotocin and 120 mg/kgBW nicotinamide. Measurement of TIM thickness was conducted using a Leica light microscope with hematoxylin-eosin staining. The results showed no statistically significant differences among the groups (p = 0.051), although a decreasing trend in TIM thickness was observed at the 1.5 mg/gBW/day dose. In this context, dahlia tuber inulin extract demonstrated a tendency to reduce TIM thickness in T2DM-induced rats.

KEYWORDS:
dahlia tuber, intima-media thickness, inulin, type 2 diabetes mellitus.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder influenced by genetic, environmental, and lifestyle factors, with its primary etiology involving impaired β-cell insulin secretion and insulin resistance in target tissues.[1] The global prevalence of T2DM continues to rise. The International Diabetes Federation (IDF) reported that in 2025 there were 589 million individuals living with diabetes worldwide, and this number is projected to reach 700 million by 2045.[2] T2DM accounts for approximately 90% of all diabetes cases, with the most significant increases observed in developing countries such as India and China.[3] Based on the results of the 2023 Survei Kesehatan Indonesia (SKI), the prevalence of diabetes mellitus, as determined by blood sugar level examinations, in the population aged 15 years and above was 11.7%.[4]

Globally, T2DM is a major cause of morbidity and mortality and is strongly associated with long-term complications, particularly cardiovascular diseases.[5]

Atherosclerosis is one of the most serious cardiovascular complications frequently occurring in

patients with T2DM. The condition develops through multiple mechanisms, including endothelial dysfunction, chronic inflammation, oxidative stress, and lipid metabolism disturbances triggered by prolonged hyperglycemia.[6] In the early stages of atherosclerosis, thickening of the intima-media layer of arterial walls occurs as a response to endothelial injury and lipid infiltration. This thickening, including in the thoracic aorta, reflects structural vascular alterations underlying atheromatous plaque formation. Intima-media thickness has long been recognized as an early indicator and a predictive marker for cardiovascular events such as myocardial infarction and ischemic stroke.[7]

Chronic hyperglycemia in diabetes directly damages blood vessels by inducing oxidative stress and endothelial dysfunction, resulting in impaired regulation of blood flow and increased susceptibility to inflammation. Persistent hyperglycemia elevates reactive oxygen species (ROS) and activates detrimental metabolic pathways, such as AGE-RAGE signaling, which decrease nitric oxide availability, initiate inflammation, and contribute to vascular stiffness and a pro-thrombotic state. This endothelial injury represents a critical early event that connects diabetes to macrovascular complications, such as atherosclerosis.[8] A study by Ismawati et al. (2022) demonstrated that in an atherosclerotic rat model, intima-media thickness increased progressively with disease advancement, reflecting dynamic vascular responses to multiple risk factors.[9] In T2DM, atherosclerosis significantly elevates the risk of ischemic stroke, particularly when compounded by lifestyle factors that accelerate plaque formation and arterial narrowing.[10]

Inulin is a polysaccharide composed of fructose chains that serves as an energy source for gut microbiota. Fermentation of inulin by intestinal bacteria produces short-chain fatty acids (SCFAs), which play a role in reducing mucosal inflammation. Numerous studies have investigated the potential benefits of inulin in pathological conditions such as diabetes mellitus and atherosclerosis.[11, 12] A study by Ismawati et al. (2024) reported that inulin derived from dahlia tubers reduced insulitis and HOMA-IR in type 2 diabetic rats after 21 days of administration. Although it did not increase insulin expression, inulin improved insulin sensitivity and reduced inflammation in the pancreatic islets, suggesting its potential role in preventing vascular complications such as atherosclerosis.[11]

To date, research investigating the vascular effects of dahlia tuber inulin in type 2 diabetes remains highly limited, particularly regarding the evaluation of thoracic aortic intima-media thickness as an early marker of atherosclerosis. Research showed that administering inulin extract from dahlia tubers can prevent the formation of atherosclerotic lesions in the coronary arteries[13]. In this study, atherosclerotic lesions were assessed using a

coronary artery tissue scoring system. Although this assessment is sensitive, its limitation is its invasive nature, which makes it difficult to use. Atherosclerosis assessment by measuring the thickness of the thoracic aorta (IMT) can also detect subclinical atherosclerosis and is non-invasive[14]. The findings of this research are expected to contribute to the scientific development of natural-based therapeutic strategies aimed at preventing atherosclerotic progression in T2DM. Therefore, this study aimed to evaluate the effects of dahlia tuber inulin extract on thoracic aortic intima-media thickness in male Wistar rats induced with type 2 diabetes mellitus.

METHODS

This study was a continuation of previous research on the utilization of inulin extract.[13] Dahlia tubers were sourced from Bukittinggi, West Sumatra Province, Indonesia. The extraction procedure began by heating 2500 g of cleaned and finely sliced fresh dahlia tubers in 5000 ml of distilled water for 30 minutes at 80–90°C. The solution was then cooled to room temperature and filtered to separate the filtrate and residue. Ethanol was added to the filtrate in a 1:1 (v/v) ratio, followed by cooling at 4°C for 18 hours. The mixture was centrifuged at 9000 rpm for 10 minutes to obtain a white inulin precipitate, which was subsequently dried at 60°C until yellowish-white inulin powder was formed. Ethical approval for this study was granted by the Health Research Ethics Unit, Faculty of Medicine, Universitas Riau, under certificate number 079/UN19.5.1.1.8/UEPKK/2025. This experimental research, using a post-test-only control group design, was conducted at the Biochemistry Laboratory and the Anatomical Pathology Laboratory, Faculty of Medicine, Universitas Riau. The research activities and data collection were carried out from July to November 2025.

Male Rattus norvegicus Wistar strain aged 2–3 months and weighgted 200–250 grams. The health of the rats was carefully looked after, and their enclosures underwent daily cleaning. The independent variable was dahlia tuber inulin extract, while the dependent variable was the histopathological profile of the coronary artery. The controlled variable was the use of male Wistar Rattus norvegicus. A total of 20 rats were divided to five groups. Group I was designated as the normal control; Group II was the group with diabetes induced by STZ; and the other three treatment groups were diabetes induced by STZ with inulin extract at doses of 0.5 mg/gBW/day, 1 mg/gBW/day, and 1.5 mg/gBW/day, respectively. Prior to treatment, the animals underwent a 12-hour fasting period. They then received an intraperitoneal injection of streptozotocin (STZ) at a dose of 60 mg/kgBW dissolved in 0.1 M citrate buffer (pH 4.5). Nicotinamide (NA) was administered 15 minutes after STZ injection at a dose of 120 mg/kgBW. 8

After 72 hours, blood specimens were obtained from the tail vein. Rats were identified as having diabetes when their blood glucose measurements went above 250 mg/dL, and they then participated in the inulin treatment phase. The rats received inulin by oral gavage once daily for 21 days.

The thoracic aorta was excised after anesthesia with ether, and the tissue was rinsed with NaCl solution before being processed into histological preparations using (hematoxylin eosin) HE staining. The microscopic slides were evaluated by an anatomical pathologist under a light microscope at 400× magnification across nine fields of view, and the mean value was recorded. The intima–media thickness was quantitatively measured using LAS EZ software integrated with a Leica microscope, and the data were subsequently analyzed using the Statistical Package for the Social Sciences (SPSS). As the data were not normally distributed, comparisons between groups were performed using the non-parametric Kruskal–Wallis test to assess differences among treatment groups.

RESULT AND DISCUSSION

Inulin was obtained using an extraction method. Analysis of its basic components revealed a moisture content of 6.75%, ash content of 0.39%, crude protein of 0.95%, fat content of 0.49%, carbohydrate content of 91.41%, and natural fiber of 0.97%.

The results showed that the highest mean tunica intima-media thickness was found in Group IV (0.13 ± 0.02 mm), while the lowest mean value was observed in Group V (0.11 ± 0.03 mm). (Figure 1)

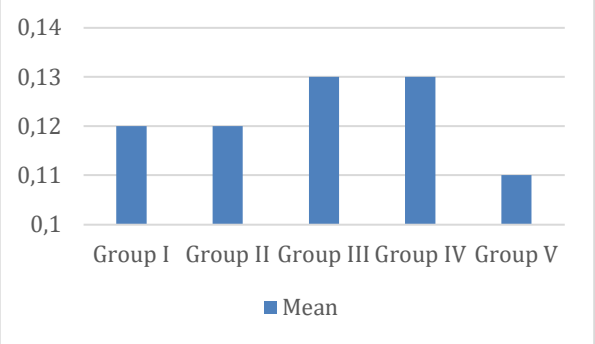

Figure 1. Average results of the thoracic aorta intima-media thickness (IMT) measurements from each treatment group. Group I is a control rat without treatment, Group II is DM, Group III is DM + 0.5 mg/gBW/day inulin extract, Group IV is DM + 1 mg/gBW/day inulin extract, and Group V is DM + 1.5 mg/gBW/day inulin extract.

The Kruskal–Wallis test performed using SPSS showed a p-value of 0.124 ($p > 0.05$), indicating no statistically significant differences in thoracic aorta intima–media thickness among the treatment groups. Although the differences were not statistically significant, the results indicated a tendency toward decreased intima–media thickness in the group receiving 1.5 mg/gBW/day dahlia tuber inulin extract compared with the untreated diabetic group. **Figure 2** illustrates the intima–media thickness of the thoracic aorta in each treatment group, highlighting the observable trend of reduced thickness in the inulin-treated groups.

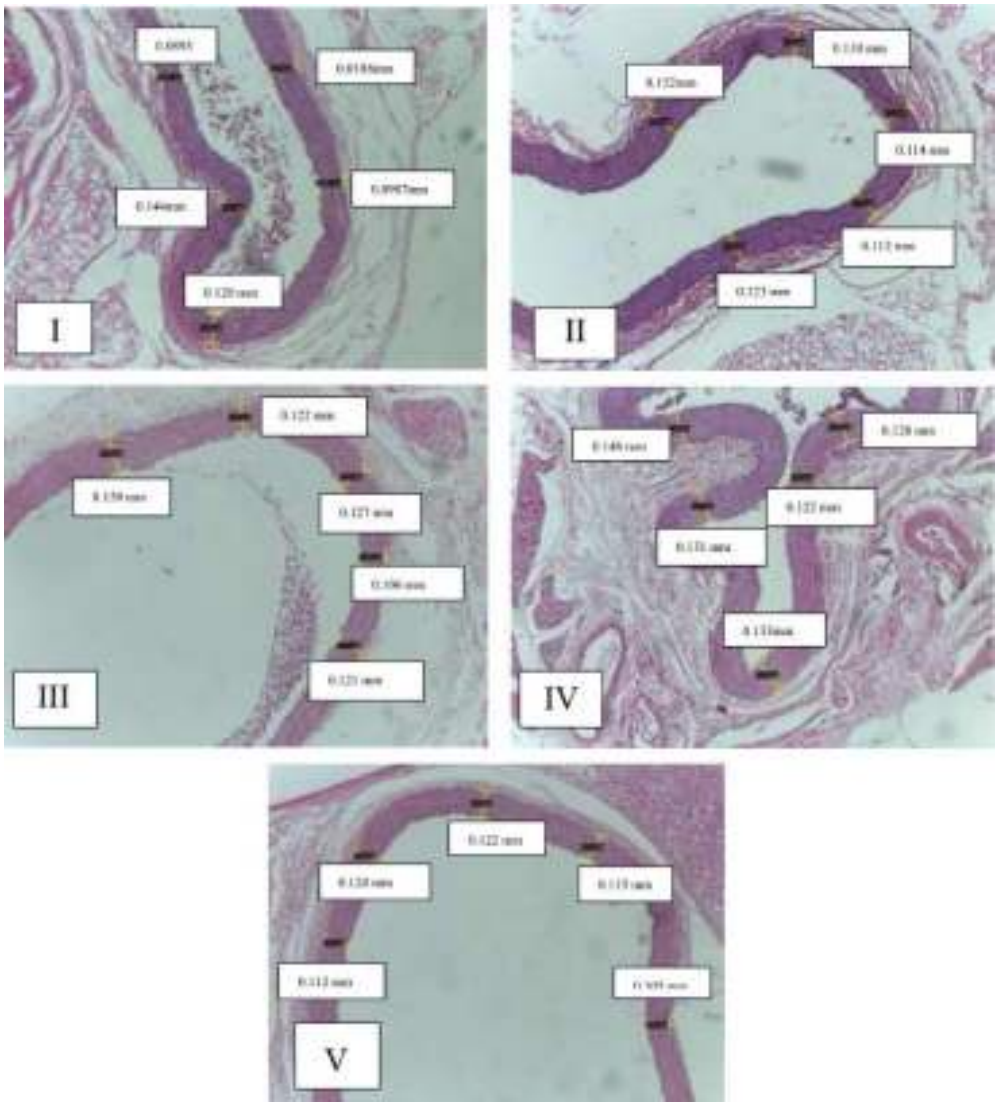

Figure 2. Histopathological images of the thoracic aorta show the thickness of the intima-media (IMT) in all treatment groups (HE staining, magnification 100x). Group I is a control rat without treatment, Group II is DM, Group III is DM + 0.5 mg/gBW/day inulin extract, Group IV is DM + 1 mg/gBW/day inulin extract, and Group V is DM + 1.5 mg/gBW/day inulin extract.

These findings contrast with those of Ismawati et al. (2025), who reported significant differences in atherosclerosis scoring in the coronary artery.[13] The non-significant differences observed in this study may be attributed to the inherent characteristics of the thoracic aorta and the method of evaluating atherosclerosis used[14]. As described by Arridho et al. (2017), the thoracic aorta is a blood vessel segment with stable laminar flow, which provides an atheroprotective effect, making the development of atherosclerosis less likely in this region compared to other vascular segments. Therefore, the location of the examined tissue strongly influences the results, and the use of the thoracic aorta, which experiences stable hemodynamics, may explain why diabetes induction did not result in histopathological changes.[15]

In early diabetic atherosclerosis, plaque formation is driven by hyperglycemia-induced endothelial dysfunction, oxidative stress, and

inflammation, leading to localized lipid-rich lesions that increase histological lesion scores before overall wall thickening occurs.[16] This means lesion scoring—which reflects focal plaque severity—is more sensitive to early atherogenic changes than global measurements like intima–media thickness (IMT). IMT represents broad structural remodeling of the vessel wall and may not change significantly in early stages or in arteries such as the thoracic aorta despite active atherogenesis elsewhere. Evidence also shows that diabetic vascular disease tends to produce more inflamed and necrotic plaques in coronary arteries—features captured by lesion scoring—while IMT changes, especially in large vessels, progress more slowly and may remain similar between diabetic and non-diabetic groups in early experiments. Thus, early localized atherosclerotic lesions can differ between groups even when IMT does not.[17]

This study evaluated three doses of dahlia tuber inulin extract (0.5, 1, and 1.5 mg/gBW) and found no significant effect on thoracic aorta intima-media thickness in type 2 diabetic rats. These findings contrast with Ismawati et al. (2025), who reported that inulin significantly reduced atherosclerosis scores in the coronary arteries by decreasing foam cells and improving vascular histopathology. The discrepancy may be attributed to differences in the blood vessel studied; the protective effects of inulin appear more pronounced in advanced stages, when inflammation and plaque formation are already established.

These findings are consistent with literature indicating that the effects of inulin on vascularization depend on administration duration, chain structure, dose, and animal model. In ApoE$^{-/-}$ mice, short- and long-chain inulin administered for 12 weeks significantly reduced atherosclerotic plaque formation through improved lipid metabolism, decreased vascular inflammation, and modulation of gut microbiota, whereas in APOE*3-Leiden mice, inulin was reported to accelerate atherosclerosis.[18,19] This highlights that inulin's vascular effects are influenced by genetic background, metabolic status, and exposure duration. Therefore, the absence of changes in thoracic aorta intima-media thickness in this study may be attributed to the short treatment duration and the atheroprotective nature of the thoracic aorta.

CONCLUSION

Dahlia tuber inulin extract demonstrated a trend toward reducing thoracic aortic tunica intima-media thickness in type 2 diabetic rats, especially at the highest dose; however, these differences were not statistically significant.

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