Nutr Res Pract. 2024 Feb;18(1):88-97
https://doi.org/10.4162/nrp.2024.18.1.88
pISSN 1976-1457·eISSN 2005-6168

Nutrition Research and Practice

Original Research

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Daraesoon (shoot of hardy kiwi) mitigates hyperglycemia in db/db mice by alleviating insulin resistance and inflammation

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OPEN ACCESS

Received: Dec 13, 2023
Revised: Jan 10, 2024
Accepted: Jan 17, 2024
Published online: Jan 25, 2024

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Funding
This research was supported by the Globalization of Korean Foods R&D program, funded by the Ministry of Agriculture, Food and Rural Affairs, Republic of Korea.

Conflict of Interest
The authors declare no potential conflicts of interests.

Author Contributions
Conceptualization: Kim JI; Formal analysis: Choi HN; Funding acquisition: Kim JI;

ABSTRACT

BACKGROUND/OBJECTIVES: Mitigating insulin resistance and hyperglycemia is associated with a decreased risk of diabetic complications. The effect of Daraesoon (shoot of hardy kiwi, *Actinidia arguta*) on hyperglycemia was investigated using a type 2 diabetes animal model.
MATERIALS/METHODS: Seven-week-old db/db mice were fed either an AIN-93G diet or a diet containing 0.4% of a 70% ethanol extract of Daraesoon, whereas db/+ mice were fed the AIN-93G diet for 7 weeks.
RESULTS: Consumption of Daraesoon significantly reduced serum glucose and blood glycated hemoglobin levels, along with homeostasis model assessment for insulin resistance in db/db mice. Conversely, Daraesoon elevated the serum adiponectin levels compared to the db/db control group. Furthermore, Daraesoon significantly decreased both serum and hepatic triglyceride levels, as well as serum total cholesterol levels. Additionally, consumption of Daraesoon resulted in decreased hepatic tumor necrosis factor-α and monocyte chemoattractant protein-1 expression.
CONCLUSIONS: These results suggest that hypoglycemic effect of Daraesoon is mediated through the improvement of insulin resistance and the downregulation of pro-inflammatory cytokine expression in db/db mice.

Keywords: *Actinidia arguta*; insulin resistance; adiponectin; inflammation; db/db mice

INTRODUCTION

In low and middle-income countries, one in every ten individuals aged between 20 and 79 is diagnosed with diabetes mellitus (DM), with over 90% developing type 2 diabetes mellitus (T2DM) [1]. T2DM is characterized by insulin resistance, which leads to insufficient insulin action and resultant hyperglycemia [2]. Insulin resistance entails a reduced responsiveness of target organs to insulin, causing inadequate suppression of hepatic glucose production and diminished glucose uptake in peripheral tissues, such as skeletal muscle and adipose tissue [2,3]. Obesity induces low-grade systemic chronic inflammation [4]. Obese adipose tissue increased release of pro-inflammatory adipokines, which can cause insulin resistance either directly by interfering with the insulin signaling pathway or indirectly by stimulating inflammatory pathways [5]. In addition, visceral fat accumulation in obesity is associated with reduced secretion of adiponectin, a molecule involved in anti-inflammatory and insulin sensitivity mechanisms [6].

Investigation: Kim JI; Methodology: Choi HN, Kim JI; Supervision: Kim JI; Writing – original draft: Choi HN; Writing – review & editing: Choi HN, Kim JI.

Treatment strategies for diabetes primarily aim at regulating hyperglycemia to maintain blood glucose levels within normal or near normal range, as this can mitigate the risk of diabetic complications and enhance overall well-being [7]. Chronic hyperglycemia primarily induces intracellular oxidative stress through the polyol pathway and the formation of advanced glycation end products (AGEs) [8,9]. The polyol pathway facilitates the conversion of glucose to sorbitol, which in turn depletes nicotinamide adenine dinucleotide phosphate (NADPH) and diminishes glutathione production, thereby exacerbating oxidative stress [9]. The AGEs modify plasma proteins, and the altered plasma proteins interact with the AGE receptor on endothelial cells, triggering the generation of reactive oxygen species (ROS) [8,9]. The oxidative stress-mediated damage ensuing from these processes plays a pivotal role in development and progression of diabetic complications [10].

Insulin resistance promotes the synthesis of triglycerides (TGs) in the liver, leading to serum lipid accumulation and subsequent dyslipidemia [2,11,12]. Dyslipidemia significantly contributes to cardiovascular complications, a major cause of morbidity and mortality in individuals with T2DM [13]. The low-grade inflammation in diabetes also increases the risk for cardiovascular diseases (CVDs), including atherosclerosis, since it induces endothelial dysfunction, leading to an increase in vascular permeability and foam cell formation [14,15].

Actinidia arguta, commonly referred to as hardy kiwi, grows wild in the mountains of Northeast Asian countries, including Korea, and belongs to the genus *Actinidia* of the family *Acinidiaceae* [16]. The fruit of *A. arguta* is a good source of polyphenols, vitamin C, carotenoids, dietary fiber, organic acids and minerals [16,17]. The roots, stems, and leaves of this plant are widely used as herbal medicine material [16,17]. The young leaves of *A. arguta,* known as Daraesoon, are specifically harvested in spring for culinary use. Once harvested, Daraesoon can be boiled, dried, and stored to serve as a vegetable ingredient throughout the year [18]. The preparation of dried Daraesoon involves soaking it in water, boiling, and subsequently immersing it in water prior to its use as a culinary ingredient.

The ethanolic extract of Daraesoon was previously found to show a higher total phenolic content compared to other parts of *A. arguta*, such as fruits, flowers, and stems [17]. The Daraesoon extract showed strong α-glucosidase inhibitory activity *in vitro*, and reduced postprandial hyperglycemia in streptozotocin-treated rats, an effect analogous to that of acarbose [18,19]. Chronic feeding of the Daraesoon extract ameliorated fasting hyperglycemia in mice fed with a high fat, high sucrose (HFHS) diet [18]. The ethanol extract of Daraesoon inhibited activities of 5-lipoxygenase (Lox) and cyclooxygenase (COX)-2 *in vitro*, demonstrating anti-inflammatory effect [20]. The 75% ethanol extract of Daraesoon suppressed nitric oxide (NO) synthesis in Raw 264.7 cell treated with lipopolysaccharide (LPS) [21].

Daraesoon may thus confer potential benefits in ameliorating hyperglycemia and inflammation; however, only a few animal studies have been conducted to elucidate its effects. In addition, the effects of Daraesoon on inflammatory cytokines and adiponectin secretion remain inadequately explored in animal study. The leptin receptor deficient db/db mice show increased body weight, hyperglycemia, insulin resistance, and dyslipidemia [22], making them a common model for studying obesity and T2DM [23]. Accordingly, this study aims to assess the effects of Daraesoon supplementation on insulin resistance, hyperglycemia, and inflammation in db/db mice, a type 2 diabetic animal model.

https://doi.org/10.4162/nrp.2024.18.1.88

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MATERIALS AND METHODS

Preparation of Daraesoon extract

Dried Daraesoon was purchased from National Forestry Cooperative Federation (Yeoju, Korea). Daraesoon was first soaked in cold water for 16 h, then boiled for 30 min. After that, Daraesoon was immerseded in cold water for 1 h. Then, excess water was removed, and the material was freeze-dried. The resulting powdered Daraesoon was extracted twice at room temperature for 24 h using 20 times of 70% ethanol, and filtered using Whatman No. 1 paper (GE Healthcare, Chalfont St. Giles, UK). A rotary evaporator was used to remove extraction solvents at 40°C (Eyela, Tokyo, Japan). The extraction yield was 8.3%.

Animal experiments

All animal procedures were approved by the Laboratory Animal Resource Center of Inje University, Korea (approval No. 2013-18). Male C57BL/KsL-db/db mice and their lean heterozygote littermates (db/+) mice (6 weeks of age) were purchased from the Korea Research Institute of Bioscience and Biotechnology (Cheongju, Korea), and provided solid diet *ad libitum* during one-week for adaptation. All animals were maintained under well-controlled conditions at a temperature of 21 ± 2°C and a relative humidity of 55 ± 5% with a regular 12:12 h light–dark cycle. After one-week adaptation, male db/db mice were randomly divided into a control group (n = 7; receiving AIN-93G diet) and a Daraesoon group (n = 7; AIN-93G diet containing 0.4% Daraesoon extract).

The concentration of Daraesoon extract used to make the animal diet was chosen based on previous study showing that the long-term consumption of 70% ethanol extract of Daraesoon (0.4% of the diet) ameliorates hyperglycemia in mice fed with a HFHS diet [18]. The lean heterozygote littermates (normal control group; n = 7) were administered an AIN-93G diet for 7 weeks. The compositions of diets of all groups are shown in **Table 1**.

Biochemical assays and hepatic lipid profiling

After 7 weeks, all animals were fasted overnight, and sacrificed via cardiac puncture to collect blood and organ samples. The blood samples were then centrifuged at 3,000 g for 15 min at 4°C (Eppendorf Centrifuge 5415R; Eppendorf, Hamburg, Germany). The liver and serum samples were immediately stored at −70°C. Blood glycated hemoglobin levels were measured using EASY A1c (Infopia Co., Anyang, Korea). Serum glucose, TG, total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) levels were analyzed using commercial

Table 1. Composition of basal and experimental diets

Ingredient	Groups		
	Lean control (%)	db/db control (%)	Daraesoon (%)
Corn starch	39.80	39.80	39.40
Casein	20.00	20.00	20.00
Dextrinized cornstarch	13.20	13.20	13.20
Sucrose	10.00	10.00	10.00
Soybean oil	7.00	7.00	7.00
Alpha-cellulose	5.00	5.00	5.00
Mineral mixture[1)]	3.50	3.50	3.50
Vitamin mixture[2)]	1.00	1.00	1.00
L-cystine	0.30	0.30	0.30
Choline bitartrate	0.25	0.25	0.25
tert-butyl hydroquinone	0.0014	0.0014	0.0014
Daraesoon extract	-	-	0.4

[1)]AIN-93G vitamin mixture; [2)]AIN-93G mineral mixture.

https://doi.org/10.4162/nrp.2024.18.1.88

kits using enzymatic method (Asan Pharmaceutical, Seoul, Korea). Serum insulin and adiponectin levels were measured using commercial enzyme-linked immunosorbent (ELISA) assay kits. Insulin and adiponectin ELISA kits were purchased from Mercodia (Uppsala, Sweden) and BioVendor Co. (Modrice, Czech Republic), respectively. Homeostasis model assessment for insulin resistance (HOMA-IR) value was calculated using the formula [24]:

$$\text{HOMA-IR} = \{\text{Insulin } (\mu\text{U/mL}) \times \text{Glucose (mmol/L)}\}/22.5$$

Hepatic total lipids were extracted using Folch *et al.* [25] method. After extraction, hepatic TG content was measured using the same kits used for measuring the serum TG. All kits were used following the manufacturer's instructions.

Western blot

For western blotting, the frozen liver tissues were homogenized in protein lysis buffer (PRO-PREPTM, Intron Biotechnology, Seongnam, Korea), and then centrifuged (13,000 g at 4°C for 30 min). After the supernatants of the liver lysates were collected, their respective protein contents were determined using a bicinchoninic acid protein assay kit (Thermo Fisher Scientific, Rockford, IL, USA). The 50 μg of total protein were loaded on 12% sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and transferred to polyvinylidene difluoride membranes (Bio-Rad Laboratories, Hercules, CA, USA). The membranes were blocked with 5% (w/v) bovine serum albumin (BSA) in Tris-buffered saline containing 0.1% Tween 20 (TBS-T) for 2 h at room temperature. The blocked membranes were then incubated overnight with diluted primary antibodies (diluted 1:1,000 with 5% BSA in TBS-T) at 4°C. Primary antibodies used include monocyte chemoattractant protein 1 (MCP-1) and anti-tumor necrosis factor alpha (TNF-α; Cell Signaling Technology, Danvers, MA, USA). After washing with 1× TBS-T, the membrane was incubated with goat anti-rabbit-horseradish peroxidase secondary antibody (Santa Cruz Biotechnology, Dallas, TX, USA) for 3 h at 4°C. The bands were detected using enhanced chemiluminescence kit (GE Healthcare). Target protein expression was normalized to that of β-actin.

Statistical analyses

The results are presented as means ± standard error of the mean (SEM). A one-way analysis of variance was used to evaluate statistical significance of differences among the groups, followed by Tukey's test. The results were deemed to have statistical significance at a significance level of $P < 0.05$ (SAS ver. 9.2; SAS Institute, Cary, NC, USA).

RESULTS

Body weight and food intake

Table 2 presents the initial and final body weights, along with food intake indices of animals across the 3 groups. Compared to the lean control group, the db/db control group, and the Daraesoon group exhibited significant increases in final body weight, weight gain, food intake, and feed efficiency ratio (FER). However, the values between the db/db control and Daraesoon groups were not significantly different.

Effect of Daraesoon on glycemic control and insulin resistance

Glycemic control and insulin resistance indices are shown **Table 3**. The diabetic control group exhibited significantly higher levels of glycated hemoglobin, glucose, insulin and HOMA-

https://doi.org/10.4162/nrp.2024.18.1.88

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Table 2. Body weight, food intake, and feed efficiency ratio of db/db mice

Variables	Lean control group	db/db control group	Daraesoon group
Initial body weight (g)	19.6 ± 0.5^{ns}	20.5 ± 0.6	20.3 ± 0.5
Final body weight (g)	24.7 ± 0.8^{a}	41.1 ± 1.2^{b}	39.8 ± 1.3^{b}
Weight gain (g/day)	0.103 ± 0.014^{a}	0.421 ± 0.026^{b}	0.397 ± 0.026^{b}
Food intake (g/day)	3.3 ± 0.2^{a}	4.3 ± 0.2^{b}	4.0 ± 0.2^{b}
Feed efficiency ratio[1)] (%)	3.2 ± 0.4^{a}	9.9 ± 0.6^{b}	10.1 ± 1.0^{b}

Seven-week-old db/db mice were fed an AIN-93G diet or a diet containing 0.4% Daraesoon extract, whereas lean control group was offered the AIN-93G diet *ad libitum* for 7 weeks. Values represent mean ± SEM (n = 7).
NS, not significant; SEM, standard error of the mean.
[1)]Feed Efficiency Ratio (%) = Body Weight Gain (g/day)/Food Intake (g/day) × 100.
[a,b]Means within a row not sharing a common alphabet are significantly different at $P < 0.05$.

Table 3. Glycated hemoglobin, serum glucose, insulin, adiponectin, and HOMA-IR in db/db mice

Variables	Lean control group	db/db control group	Daraesoon group
Blood glycated hemoglobin (%)	5.3 ± 0.3^{a}	8.1 ± 0.3^{c}	7.0 ± 0.3^{b}
Serum glucose (mg/dL)	105.3 ± 6.7^{a}	491.5 ± 24.6^{c}	379.5 ± 15.0^{b}
Serum insulin (μIU/mL)	21.1 ± 1.1^{a}	91.3 ± 4.7^{b}	78.4 ± 4.1^{b}
Serum adiponectin (μg/mL)	15.1 ± 0.8^{c}	9.5 ± 0.5^{a}	11.9 ± 0.6^{b}
HOMA-IR[1)]	5.5 ± 0.4^{a}	111.5 ± 9.4^{c}	73.3 ± 4.2^{b}

Seven-week-old db/db mice were fed an AIN-93G diet or a diet containing 0.4% Daraesoon extract, whereas lean control group was offered the AIN-93G diet *ad libitum* for 7 weeks. Values represent mean ± SEM (n = 7).
HOMA-IR, homeostasis model assessment for insulin resistance; SEM, standard error of the mean.
[1)]HOMA-IR = {Insulin (μU/mL) × Glucose (mmol/L)}/22.5.
[a,b,c]Means within a row not sharing a common alphabet are significantly different at $P < 0.05$.

IR compared to the lean control group. In contrast, the Daraesoon group demonstrated significantly reduced levels of glycated hemoglobin and serum glucose when compared to the db/db control group. Serum insulin levels did not show a significant difference between the db/db control and Daraesoon groups. However, consumption of Daraesoon significantly lowered HOMA-IR in db/db mice. Conversely, the db/db control group had significantly lower serum adiponectin levels compared to those in the lean control group, whereas serum adiponectin levels in the Daraesoon group were significantly higher than those in the diabetic control group.

Effect of Daraesoon on serum lipid profile and hepatic TGs

The effects of Daraesoon on serum and hepatic lipid profiles are summarized in **Table 4**. Serum TG and TC levels of the db/db control group were found to be significantly higher than those in the lean control group. However, administration of Daraesoon extract resulted in significantly lowered serum TG and TC levels compared to those in the db/db control mice. There was no significant difference in serum HDL-C levels among the 3 groups. The db/db control group showed increased hepatic TG compared with the lean control group. The Daraesoon group yielded significantly lower hepatic TG concentrations than those in the db/db control group.

Table 4. Serum and hepatic lipids in db/db mice

Variables	Lean control group	db/db control group	Daraesoon group
Serum TG (mg/dL)	75.7 ± 4.2^{a}	141.0 ± 6.3^{c}	117.5 ± 5.9^{b}
Serum TC (mg/dL)	83.3 ± 5.6^{a}	160.9 ± 9.7^{c}	125.3 ± 7.4^{b}
Serum HDL-C (mg/dL)	50.9 ± 3.0^{ns}	59.3 ± 2.8	51.6 ± 2.7
Hepatic TG (mg/g liver)	28.3 ± 1.9^{a}	56.8 ± 3.5^{c}	38.0 ± 2.1^{b}

Seven-week-old db/db mice were fed an AIN-93G diet or a diet containing 0.4% Daraesoon extract, whereas lean control group was offered the AIN-93G diet *ad libitum* for 7 weeks. Values represent mean ± SEM (n = 7).
TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; NS, not significant; SEM, standard error of the mean.
[a,b,c]Means within a row not sharing a common alphabet are significantly different at $P < 0.05$.

https://doi.org/10.4162/nrp.2024.18.1.88

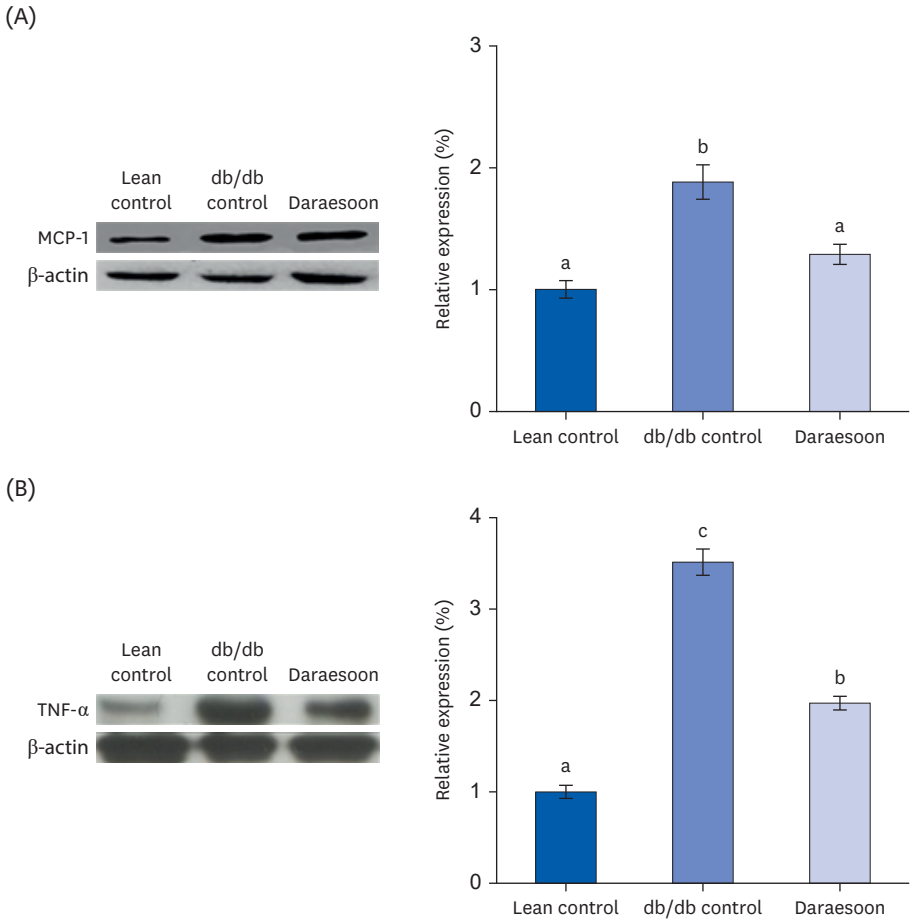

Fig. 1. Protein expression of MCP-1 (A) and TNF-α (B) of the liver in db/db mice.
Seven-week-old db/db mice were fed an AIN-93G diet or a diet containing 0.4% Daraesoon extract, whereas lean control group was offered the AIN-93G diet *ad libitum* for 7 weeks. Values represent mean ± SEM (n = 7).
MCP-1, monocyte chemoattractant protein 1; TNF-α, tumor necrosis factor α; SEM, standard error of the mean.
[a,b,c]Each bar that do not share a common letter are significantly different at $P < 0.05$.

Effect of Daraesoon on expression of hepatic pro-inflammatory cytokines

The effects of Daraesoon on pro-inflammatory cytokine proteins are shown in **Fig. 1**. The protein levels of MCP-1 and TNF-α in the db/db control group were significantly higher than those in the lean control group. These levels were significantly reduced by consumption of Daraesoon extract. Notably, no significant difference in MCP-1 expression was observed between the lean control and Daraesoon groups.

DISCUSSION

Maintaining normal blood glucose levels is crucial to the prevention of diabetic complications. We investigated the impact of Daraesoon (shoot of hardy kiwi, *A. arguta*) on hyperglycemia using a type 2 diabetes animal model. In obese prediabetes, weight loss can delay the onset or reduce the risk of T2DM, and weight loss has been shown to enhance glycemic control in patients with T2DM [26]. Our data showed that the final body weight was significantly increased in the db/db control group compared with the lean control group. However, the 70% ethanol extract of Daraesoon (0.4% of the diet) did not significantly affect

https://doi.org/10.4162/nrp.2024.18.1.88

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body weight in db/db mice. A previous study reported that consuming a HFHS diet, including 70% ethanol extract of Daraesoon at a rate of 0.4%, was not found to affect body weight in mice, which is consistent with our data [18].

Long-term consumption of Daraesoon extract led to reduced serum glucose and glycated hemoglobin levels in db/db mice, indicating improved long-term blood glucose control in this study. Previous studies have demonstrated α-glucosidase inhibitory activity of Daraesoon *in vitro* and *in vivo* [18]. Furthermore, the chronic consumption of Daraesoon extract resulted in lower serum glucose levels in mice given a HFHS diet, an animal model of diet-induced T2DM [18]. Pinoresinol diglucoside isolated from Daraesoon was found to be the active component that exhibits α-glucosidase inhibition capacity [19]. Pinoresinol isolated from sesame seeds was shown to demonstrate α-glucosidase inhibition *in vitro* [27]. Therefore, Daraesoon likely alleviated hyperglycemia through α-glucosidase inhibition in db/db mice in this study. It is necessary to determine the concentration of pinoresinol diglucoside in Daraesoon in further study.

Our findings also indicated that the Daraesoon group showed increased levels of serum adiponectin and reduced levels of HOMA-IR, an indicator of insulin resistance. Adiponectin mediates anti-diabetic effects by improving insulin sensitivity [28]. Adiponectin activates adenosine monophosphate-activated protein kinase (AMPK) and p38 mitogen-activated protein kinases, leading to glucose uptake and fatty acid oxidation. In addition, adiponectin promotes peroxisome proliferator-activated receptor (PPAR)-α, leading to increased energy consumption in the peripheral insulin target tissues [29]. Elevated serum adiponectin levels were previously also found to ameliorate insulin resistance and hyperglycemia in diabetic mice [30,31]. Therefore, Daraesoon likely ameliorated hyperglycemia and insulin resistance by suppressing α-glucosidase activity and increasing serum adiponectin levels in this study.

Insulin resistance increases lipolysis in adipocytes, leading to the release of circulating free fatty acids (FFAs) [11]. The increased FFAs are then taken up by the liver, and contribute to increased hepatic production of TGs and secretion of very low-density lipoprotein (VLDL) into the bloodstream [12]. Increase in TG-rich VLDL in blood circulation is considered a risk factor for diabetic atherogenic dyslipidemia [2,11]. It has been reported that 32% of type 2 diabetic patients have CVD [32]. Our study showed that Daraesoon extract supplementation alleviated TG accumulation in the liver and reduced serum TG and TC levels in the db/db mice, suggesting its potential for preventing cardiovascular complications. Natural phenolic compounds are known to ameliorate hepatic steatosis by enhancing AMPK phosphorylation [33]. The activation of AMPK by these compounds acts as a downstream regulator of sterol regulatory element-binding protein (SREBP)-1c. Inhibition of SREBP-1c results in down-regulation of *de novo* lipogenesis genes, including acetyl-CoA carboxylase, fatty acid synthase, and stearoyl-CoA desaturase [34]. Total phenolic content and total flavonoids content of the alcoholic extract of *A. arguta* leaves were reported to be 441 and 318 mg gallic acid equivalent (GAE)/g, respectively, suggesting that it could be considered a valuable health-promoting source [35]. Consequently, Daraesoon, being rich in phenolic compounds, has the potential to mitigate hepatic steatosis and dyslipidemia via AMPK activation. Further study could be needed to determine the effect of Daraesoon on AMPK phosphorylation.

Obesity-induced low-grade inflammation has been reported as a key factor in the initiation of insulin resistance and the development of T2DM [36,37]. Inflamed adipose tissue in obesity releases pro-inflammatory cytokines, which in turn lead to impairment of insulin signaling

https://doi.org/10.4162/nrp.2024.18.1.88

[36]. Obesity-induced adipocyte lipolysis upregulates the expression of nuclear factor kappa B (NF-κB), and subsequently results in increased expression of TNF-α [36]. NF-κB also activates TNF-α mediated MCP-1 expression, which lead to inhibition of insulin receptor substrate-1 and reduction of glucose uptake [36]. The systemic circulation of TNF-α and MCP-1 also induces non-alcoholic fatty liver diseases (NAFLD), since TNF-α mediates the early stage of NAFLD via fat accumulation, whereas MCP-1 induces liver infiltration, promoting progression of liver disease to advanced stages [37].

In NAFLD, TNF-α is produced by Kupffer cells (KCs) in the liver and immune cells infiltrating the liver during steatosis [38]. Additionally, TNF-α, originating outside the liver such as immune cells infiltrating expanded adipose tissues in obesity, is transported to the liver through systemic circulation. TNF-α plays a potential key role in the development and progression of NAFLD by inducing transcription of target genes involved in inflammation and causing insulin resistance [38]. Liu and colleagues' study [39] also noted increased serum levels and hepatic expression of TNF-α in mice with non-alcoholic steatohepatitis (NASH) induced by a methionine- and choline-deficient diet. Numorous studies have shown that compounds that reduce circulating TNF-α levels or its hepatic expression improve NAFLD [38].

In the early stages of NAFLD, hepatic macrophages expand rapidly and produce MCP-1, which increases hepatic infiltration of monocyte-derived macrophages, promoting steatohepatitis [40]. Zhong *et al.* [41] demonstrated an augmentation in the infiltration of hepatic macrophages and elevation of MCP-1 expression in the liver and its concentration in the bloodstream in high-fat diet-induced NAFLD animals. Upregulation of MCP-1 expression in the liver contributed to an increase in plasma MCP-1, which aggravated liver steatosis in animals fed a high-fat, high-cholesterol diet [42]. Haukeland *et al.* [43] reported that serum MCP-1 concentrations were increased in patients with NAFLD, and hepatic mRNA expression of MCP-1 was enhanced in patients with simple steatosis and NASH compared with healthy subjects.

Our findings also showed increased hepatic MCP-1 and TNF-α levels in diabetic obese mice, which were reduced upon consumption of Daraesoon extract. Ravipati *et al.* [44] reported that *A. arguta* extract has strong anti-inflammatory activities through inhibition of nitric oxide and TNF-α production *in vitro* without affecting cell viability. Caffeoyl-threonic acid and salvianic acid A purified from Daraesoon were identified to be anti-inflammatory compounds [21]. The improvement in insulin resistance and fatty liver by Daraesoon extract supplementation could be partly due to reduction in the expression of pro-inflammatory cytokines in this study. Increased expression of adiponectin also inhibits NF-κB by activating AMPK, and thereby ameliorates the inflammatory status [45]. Therefore, increased adiponectin levels upon Daraesoon consumption may alleviate inflammation.

In conclusion, Daraesoon effectively decreased the serum glucose levels and ameliorated insulin resistance, hepatic steatosis, and dyslipidemia in db/db mice through upregulation of serum adiponectin levels and downregulation of pro-inflammatory cytokine expression in the liver. Thus, Daraesoon may serve as a beneficial natural product for managing T2DM.

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