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Original Article

Hydroalcoholic extract of *Allium eriophyllum* leaves attenuates cardiac impairment in rats with simultaneous type 2 diabetes and renal hypertension

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Abstract

Some species of Allium family have been shown to offer cardioprotection in animal studies. This study aimed at examining possible role of oxidative stress in the cardioprotective effects of hydroalcoholic extract of *Allium eriophyllum* in rats with simultaneous type 2 diabetes and renal hypertension. Six groups of male Spargue-Dawley rats (8-10 rats each) including a sham-control, a diabetic group, a renal hypertensive group, three groups of animals with simultaneous diabetes and hypertension receiving vehicle, or the extract at 30 or 100 mg/kg/day were used. Four weeks after receiving vehicle or extract, blood pressure, fasting blood glucose, and serum superoxide dismutase and glutathione reductase levels were measured, and isolated heart studies were performed. Systolic blood pressure, fasting blood glucose, coronary effluent creatine kinase-MB, infarct size and coronary resistance of diabetic hypertensive group receiving vehicle were significantly higher than those of the sham-control group and treatment with the extract prevented the increase of these variables. Moreover, rate of rise and decrease of left ventricular pressure, left ventricular developed pressure, rate pressure product and serum levels of superoxide dismutase and glutathione reductase of diabetic hypertensive group receiving vehicle were significantly lower than those the sham-control group, and treatment with the extract prevented the decrease of these variables. The findings indicate that hydroalcoholic extract of *A. eriophyllum* leaves, possibly by an antioxidant mechanism, protected against simultaneous diabetes and hypertension-induced cardiac dysfunction.

Keywords: *Allium eriophyllum*; Diabetes; Renal hypertension; Oxidative stress; Rats; Isolated hearts

INTRODUCTION

The incidence and prevalence of hypertension and type 2 diabetes are increasing. It has been predicted that the total number of people with diabetes would rise from 171 million in 2000 to 366 million by 2030 (1,2), and the number of adults with hypertension would increase by 60% to a total of 1.56 billion by 2025. The prevalence of hypertension in diabetic patients is approximately twice as that in those without the disease (3). Moreover, coronary artery disease is much more common in diabetic hypertensive patients than in patients suffering from either of the diseases alone (4).

Epidemiological studies have shown that diets rich in fruits, herbs and spices are associated with a low risk of cardiovascular disease (5). One of such herbs, garlic (*Allium sativum*), from Alliacea family, and its preparations have been widely recognized as agents that are of benefit in prevention and treatment of cardiovascular and metabolic diseases including atherosclerosis, hyperlipidemia, thrombosis, hypertension, diabetes (6), and ischemic heart disease (7). Garlic has also been found to decrease total as well as low-density lipoprotein (LDL) cholesterol (8). Moreover, garlic did reduce blood pressure in human (9) and two-kidney, one-clip hypertensive rats, and enhanced nitric oxide synthesis in *in vivo* and *in vitro* preparations (10). It also offered antidiabetic effect, characterized by reduced serum glucose and HbA1c and increased serum insulin level

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in animals (11) and human (12). The beneficial effects of garlic or other species of Allium have been attributed to the inhibition of angiotensin converting enzyme (13,14), increased synthesis of nitric oxide (NO) (15,16), and antioxidant properties (16).

The Allium family is believed to have about 115 species. One of such species, *A. eriophyllum,* is grown in some areas of Fars Province, Iran. We have recently shown that hydroalcoholic extract of *A. eriophyllum* leaves had antihypertensive and antidiabetic effects in rats with simultaneous type 2 diabetes and renal hypertension (17). Cardiac dysfunction is a consequence of both hypertension and diabetes. Given the afterload and blood glucose lowering effects of the extract, the present study was designed to examine possible cardioprotective effects of the extract in the same model using Langendorff technique and to further examine whether antioxidant activity was involved in such effects.

MATERIALS AND METHODS

Plant collection and extract preparation

The fresh aerial parts (leaves) of *A. eriophyllum* were collected in April around the city of Noorabad, Fars Province, Iran. The exact species of the plant was identified by an herbal specialist from the Pharmacognosy Department, Faculty of Pharmacy of Shiraz University of Medical Science, and the voucher number (748) was assigned to the plant. The leaves were shade-dried and coarsely powdered. Hydroalcoholic (70% ethanol and 30% distilled water v/v) extract of *A. eriophyllum* leaves (HEAEL) was prepared using percolation method. The yield was about 30-35%.

Materials

Streptozotocin was obtained from Teva Parenteral Medicine Inc. (Irvine, CA, USA). Nicotinamide was purchased from Sigma-Aldrich Chemical Co. (Steinheim, Germany). Streptozotocin and nicotinamide were dissolved in sodium chloride (0.9%). Ketamine and Xylazine were obtained from Alfasan (Woerden, Holland). Triphenyltetrazolium Chloride (TTC) was supplied by Sigma-Aldrich Chemical Co. (Steinheim, Germany). Penicillin powder was obtained from Jaber-Ebne-Hayyan Co. (Tehran, Iran).

Animals

Forty male Sprague-Dawley rats (200-250 g) were obtained from Laboratory Animal Breeding Center, Shiraz University of Medical Sciences, Shiraz, Iran. They were kept under standard condition (light/dark cycle; 12 h, humidity; 25-35%, and temperature; 22-24 ºC) with standard rat chow and drinking water *ad libitum*. All animal procedures were approved by the Institutional Animal Care and Use Committee.

Experimental protocol and design

Rats were injected intraperitoneally with nicotinamide (110 mg/kg) and streptozotocin (65 mg/kg), or vehicle (0.9% sodium chloride). Seven days later, animals' blood glucose levels were determined using a Glucometer (Accu-check® active, Germany), and those with fasting blood glucose (FBG) higher than 126 mg/dl were considered as having type 2 diabetes (18).

Four weeks after the induction of diabetes, control and type 2 diabetic animals were subjected to sham-operation or induction of two-kidney, one clip renal hypertension by placing self-made solid Plexiglass clips on left renal arteries as previously described (19). Briefly, animals were anesthetized using ketamine (60 mg/kg) and xylazine (8 mg/kg), and through a left flank incision, left renal arteries were exposed, and dissected away from renal veins and surrounding tissues. Afterwards, plexiglass clips (internal diameter of 0.20-0.22 mm) were placed on the arteries. Antibiotic (penicillin) powder was applied to the incision sites, and abdominal wall and skin were sutured using absorbable (catgut) and non-absorbable (silk) suture materials (Ethicon, Edinburgh, UK), respectively. Sham-operated animals were subjected to a similar procedure, but no clip was placed around renal arteries. Animals were then recovered from anesthesia, and kept in cages of two rats each for 4 weeks under standard condition (19).

Starting from the day after operations, sham-control (Sham-C-Veh) and type 2 diabetic (DM-Veh) groups were assigned to receive vehicle. Animals in the renal artery-clipped group were assigned to 4 groups including a renal hypertensive group receiving vehicle (HTN-Veh) and 3 simultaneous type 2 diabetes and renal hypertensive groups receiving vehicle (DM+HTN-Veh), HEAEL at 30 mg/kg/day (DM+HTN-HEAEL30), or HEAEL at 100 mg/kg/day (DM+HTN-HEAEL100). The vehicle (1 ml distilled water) or the extract (dissolved in the same volume of the vehicle) was administered by oral gavage for the next 4 weeks.

After 4 weeks of treatment, FBG was measured using a drop of blood from animal's tails. Then, systolic blood pressure (SBP) was measured using non-invasive tail-cuff method (Chart 5.0 software, PowerLab 4/30, AD Instruments Inc., MA, Australia). Three consecutive blood pressure measurements with a difference of less than 5 mmHg were considered valid. The mean of such three measurements were recorded as a valid value of blood pressure in every occasion (19). Afterwards, animals were anesthetized using sodium thiopental (70 mg/kg). The animal chest cavities were opened, and hearts were removed and used for isolated heart (Langendorff) studies. Blood samples for measurement of serum levels superoxide dismutase (SOD), glutathione reductase (GR) were collected from blood pools of animals' chest cavities. The samples were allowed to clot for 30 min, centrifuged at 3000 rpm for 20 min, and their serum were separated and stored at -80 ºC until analysis.

Isolated heart study

The isolated heart studies were performed as previously described (20,21). Animal hearts were excised rapidly and mounted, via aorta, on a Langendorff apparatus (AD Instruments model: LE05200, PanLab, Spain), and perfused retrogradely with Krebs-Henseleit buffer with a pH of 7.4 and following composition in mmol/L: NaCl 118.0; KCl 4.7; $CaCl_2$ 2.5; $MgSO_4$ 1.2; KH_2PO_4 1.2; $NaHCO_3$ 25.0; and glucose 11.0. The buffer was kept at 37 ºC, bubbled constantly with 95 % O_2 and 5 % CO_2, and infused at a constant flow. Through the left atrium, a latex balloon was placed in the left ventricle. The balloon's catheter was connected to a PowerLab 8/30 data acquisition system (Chart 5.0 software, PowerLab 8/30, ADInstruments Inc., MA, Sydney, Australia) via a pressure transducer for continuous recording of the cardiac function. The balloon was then inflated to an end-diastolic pressure of 5-10 mmHg. The Langendorff mode was switched to constant-pressure (60 mm Hg) for the rest of the experiment. The hearts were allowed to equilibrate for 30 min, and a baseline measurement of left ventricular end systolic pressure, left ventricular end-diastolic pressure, rate of increase of ventricular pressure (+ dp/dt), rate of decrease of ventricular pressure (- dp/dt), heart rate and coronary flow were performed. The hearts were then subjected to 20 min global ischemia (zero-flow), followed by a 60 min of reperfusion. Samples of coronary effluent for the measurement of CK-MB were collected in the first minute of reperfusion, and kept frozen (-80 ºC) until analysis. The above-mentioned cardiac parameters were measured every 30 min during reperfusion. At the end of reperfusion, cardiac infarct size was determined using TTC staining (20,21).

Determination of cardiac infarct size

The hearts were cut into 2-mm-thick slices, and incubated in TTC solution (1%) at 37 ºC for 20 min. The slices were then incubated with 10% formalin for 24 h. Afterwards, they were digitalized using a digital camera (Powershot G1, Canon, Tokyo, Japan), and the infarct areas were then quantified as the percentage of total area of slices on both sides using image analysis software (Scion Image pro. 1.16, NIH, USA) (22).

Biochemical measurements

Coronary effluent creatine kinase MB (CK-MB) was determined using Pars Azmun commercial kits (Pars Azmun Co, INC, Karaj, Iran). Serum level of SOD and GR was determined using Biorexfars chemical kits (Shiraz, Iran). All procedures were performed according to the manufacturer's instructions.

Calculations and statistical analysis

Left ventricular developed pressure (LVDP) was calculated as left ventricular end-systolic pressure–left ventricular end-diastolic pressure. Coronary resistance (CR) was calculated as coronary perfusion pressure/coronary flow, and rate pressure product (RPP) was calculated as heart rate × LVDP. Data, presented as mean ± SEM, were analyzed using One-way Analysis of Variance (ANOVA), and in case of statistical significance, followed by Duncan's Multiple Range test. A P value of ≤0.05 was considered statistically significant. The data were analyzed using Sigmastat statistical software (version 3.0) (SanJose, CA, USA). The illustrations were prepared using SigmaPlot software (version 8.0) (San Jose, CA, USA).

RESULTS

Systolic blood pressure and fasting blood glucose

After 4 weeks treatment there was no significant difference between the SBP of Sham-C-Veh (118.8 ± 0.7 mmHg) and DM-Veh (120.4 ± 5.1 mmHg) groups. However, the SBP of HTN-Veh (179.9 ± 7.4 mmHg) and DM+HTN-Veh (173.0 ± 3.6 mmHg) groups were significantly higher than those of the Sham-C-Veh group. Moreover, the SBP of DM+HTN-HEAEL30 (129.0 ± 2.3 mmHg) and DM+HTN-HEAEL100 (110.2 ± 5.6 mmHg) were significantly lower than that of the DM+HTN-Veh group. Systolic blood pressure of DM+HTN-HEAEL100 group was significantly lower than that of DM+HTN-HEAEL30 group. There was no significant difference between the FBG of Sham-C-Veh and HTN-V groups (Table 1). However, FBG of DM-V and DM+HTN-Veh group were significantly higher than that of the Sham-C-Veh group. Moreover, FBG of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 were significantly lower than that of the DM+HTN-Veh group. There was no significant difference between FBG of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups (Table 1).

Isolated heart studies

Preischemia (baseline) + dp/dt of DM-Veh and DM+HTN-Veh, but not HTN-Veh groups were significantly lower than that of Sham-C-Veh group (Fig. 1). Moreover, + dp/dt of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly higher than that of DM+HTN-Veh. A similar pattern of difference was found at 30 and 60 min of reperfusion. There was no significant difference between + dp/dt of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups at preischemia, or after 30 or 60 min of reperfusion (Fig. 1).

Preischemia (baseline) -dp/dt of DM-Veh and DM+HTN-Veh, but not HTN-Veh, groups were significantly lower than that of Sham-C-Veh group (Fig. 1). Moreover, -dp/dt of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly higher than that of DM+HTN-Veh group. A similar pattern of difference was found at 30 and 60 min of reperfusion. There was no significant difference between -dp/dt of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups at preischemia, or after 30 or 60 min of reperfusion (Fig. 1).

Table 1.The values (mean ± SEM, n=8-10 each) of serum and coronary effluent biochemical markers.

Groups	FBG (mg/dl)	SOD (U/ml)	GRx (U/l)	CK-MB (U/ml)
Sham-C-Veh	111.2 ± 3.6	275.0 ± 42.8	69.3 ± 4.3	8.667 ± 0.955
DM-Veh	218.8 ± 13.6*	93.7 ± 12.7*	27.4 ± 3.6*	24.83 ± 2.56*
HTN-Veh	118.4 ± 3.1	143.5 ± 21.9	38.1 ± 3.5	10.14 ± 1.22
DM+HTN-Veh	177.4 ± 17.9*	114.0 ± 18.6*	30.3 ± 2.7*	17.28 ± 1.58*
DM+HTN-HEAEL30	108.4 ± 4.4#	257.7 ± 86.9#	62.9 ± 3.8#	7.2 ± 0.86#
DM+HTN-HEAEL100	104.2 ± 1.2#	282.6 ± 53.2#	64.8 ± 4.4#	6.5 ±1 .23#

FBG; fasting blood glucose, SOD; serum superoxide dismutase, GRx; serum glutathione reductase, CK-MB; coronary effluent creatin kinase MB, Sham-C-Veh; sham/control group receiving vehicle; DM-veh; diabetic group receiving vehicle; HTN-Veh; renal hypertensive group receiving vehicle, DM + HTN-Veh; diabetic-hypertensive group receiving vehicle, DM+HTN-HEAEL30; diabetic-hypertensive group receiving hydroalcoholic extract of *Allium eriophyllum* leaves at 30 mg/kg/day; DM+HTN-HEAEL100; diabetic-hypertensive group receiving hydroalcoholic extract of *Allium eriophyllum* leaves at 100 mg/kg/day. *;Significant difference ($P\leq$ 0.05) from Sham-C-Veh. #;Significant difference ($P\leq$0.05) from DM+HTN-Veh.

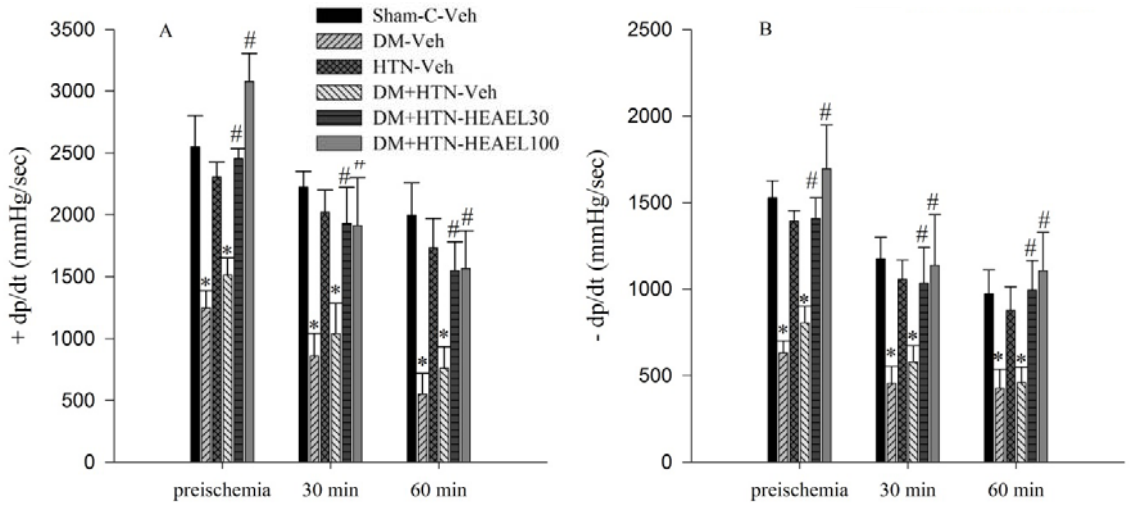

Fig. 1. A; Rate of rise (+dp/dt), and B; rate of decrease (-dp/dt) of ventricular pressure of all groups (mean ± SEM, n=6-8 in each group) at preischemia (baseline), and after 30 and 60 min of reperfusion. *; Significant difference ($P \leq 0.05$) from Sham-C-Veh. #; Significant difference ($P \leq 0.05$) from DM+HTN-Veh.

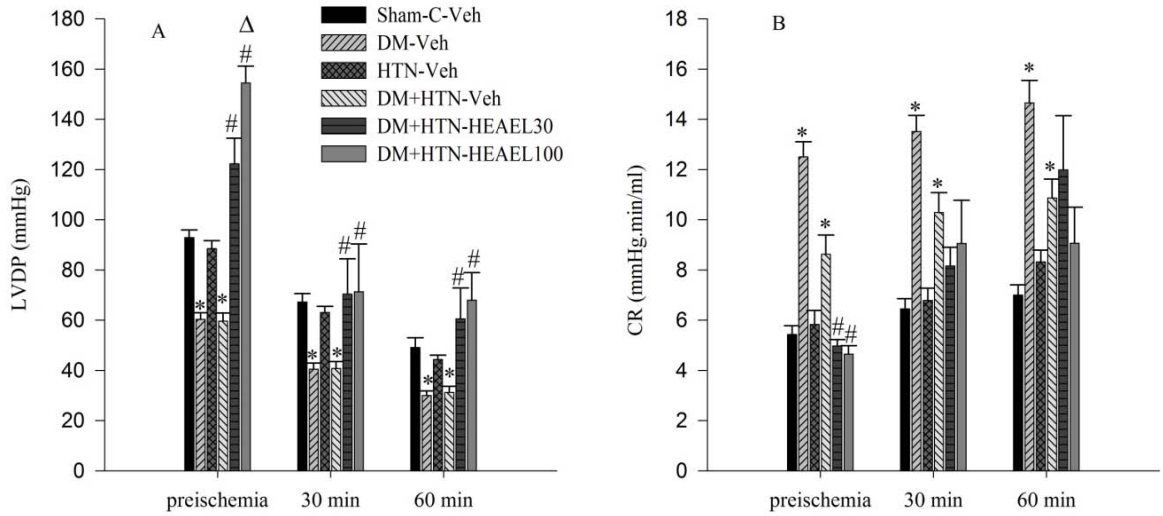

Fig. 2. A; Left ventricular developed pressure (LVDP) and B; coronary resistance (CR) of all groups (mean ± SEM, n=6-8 in each group) at preischemia (baseline), and after 30 and 60 min of reperfusion). *; Significant difference ($P \leq 0.05$) from Sham-C-Veh. #; Significant difference ($P \leq 0.05$) from DM+HTN-Veh. Δ; Significant difference ($P \leq 0.05$) from DM+HTN-HEAEL30.

Preischemia (baseline) LVDP of DM-Veh and DM+HTN-Veh, but not HTN-Veh groups were significantly lower than that of Sham-C-Veh group (Fig. 2). However, LVDP of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly higher than that of DM+HTN-Veh. A similar pattern of difference was found at 30 and 60 min of reperfusion. Left ventricular developed pressure of DM+HTN-HEAEL100 group at preischemia, but not at 30 or 60 min of reperfusion was significantly higher than that of DM+HTN-HEAEL30 group (Fig. 2).Preischemia (baseline) CR of DM-Veh and DM+HTN-Veh, but not HTN-Veh, groups were significantly higher than that of Sham-C-Veh group (Fig. 2).

The CR of DM + HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly lower than that of the DM + HTN-Veh. At 30 and 60 min of reperfusion, CR of DM-Veh and DM+HTN-Veh, but not HTN-Veh groups were significantly higher than that of Sham-C-Veh group, but there was

no significant difference between CR of DM+HTN-HEAEL30 or DM+HTN-HEAEL100 and DM+HTN-Veh groups. There was no significant difference between CR of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups at preischemia, or after 30 or 60 min of reperfusion (Fig. 2).

Preischemia (baseline) RPP of DM-Veh and DM+HTN-Veh, but not HTN-Veh groups were significantly lower than that of Sham-C-Veh group (Fig. 3). Moreover, RPP of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly higher than that of DM+HTN-Veh group. A similar pattern of difference was found at 30 and 60 min of reperfusion. Rate pressure product of DM+HTN-HEAEL100 group at preischemia and 60 min of reperfusion, but not 30 min of reperfusion, were significantly higher than that of DM+HTN-HEAEL30 group (Fig. 3).

Infarct size

Infarct sizes of DM-Veh and DM+HTN-Veh groups were significantly higher than that of Sham-C-Veh group. However, infarct sizes of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly lower than that of DM+HTN-Veh. There was no significant difference between infarct size of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups (Fig. 3).

Biochemical parameters

Serum levels of SOD and serum glutathione reductase (GRx) of DM-Veh, HTN-Veh and DM+HTN-Veh groups were significantly lower than those of Sham-C-Veh group (Table1). However, serum levels of SOD and GRx of HEAEL-treated groups (DM+HTN-HEAEL30 and DM+HTN-HEAE100) were significantly higher than those of DM+HTN-Veh groups. The concentrations of CK-MB in coronary effluent of DM-Veh and DM+HTN-Veh, but not HTN-Veh, groups were significantly higher than that of Sham-C-Veh group (Table 1). However, the levels of CK-MB of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups were significantly lower than that of DM+HTN-Veh group. There was no significant difference between SOD, GRx, or CK-MB of DM+HTN-HEAEL30 and DM+HTN-HEAEL100 groups (Table 1).

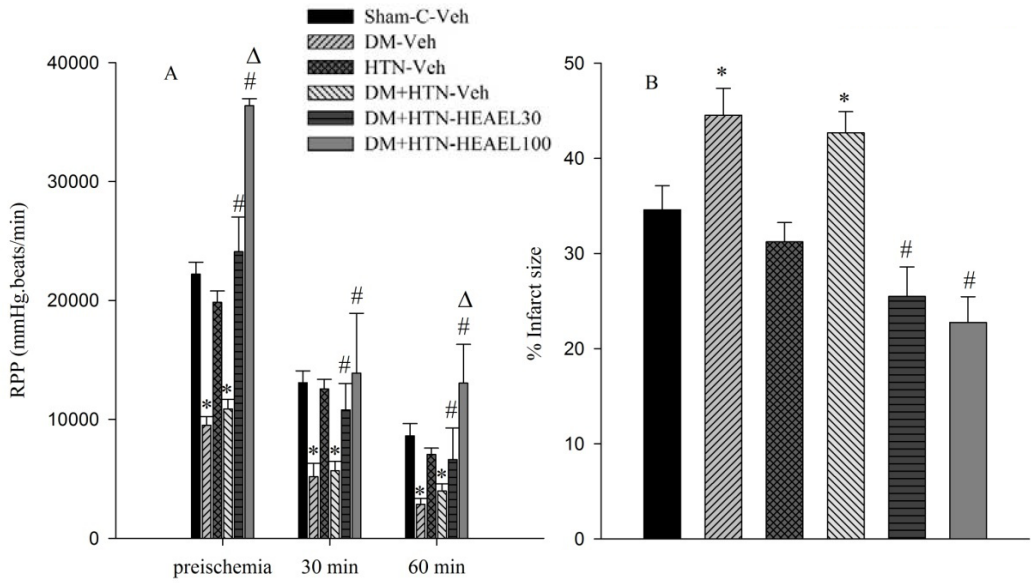

Fig. 3. A; Rate pressure product (RPP) at the preischemia (baseline) and after 30 and 60 min of reperfusion and B; infarct size (as the percentage of left ventricle) of all groups (mean ± SEM, n=6-8 in each group). *; Significant difference ($P \leq 0.05$) from Sham-C-Veh. # ; Significant difference ($P \leq 0.05$) from DM+HTN-Veh. $^{\Delta}$; Significant difference ($P \leq 0.05$) from DM+HTN-HEAEL30.

DISCUSSION

The main objective of the present study was to examine the possible cardioprotective effects of HEAEL in rats with simultaneous renal hypertension and type 2 diabetes using Langendorff technique. Our findings indicate that administration of HEAEL for 4 weeks to such rats was cardioprotective characterized by improved indices of cardiac contractility (+dp/dt), relaxation (-dp/dt), work (RPP) and damages (infarct size), and coronary vascular bed resistance. The study also shows that cardioprotective effects of HEAEL might be due to an antioxidant activity.

The findings of the study indicate that the present model of simultaneous type 2 diabetes and renal hypertension was associated with increased SBP, FBG, and impaired cardiac function characterized by decreased LVDP, +dp/dt, -dp/dt and RPP, and increased coronary resistance, infarct size, and coronary effluent CK-MB. Such findings are in agreement with our earlier (21) and other studies (23-25), and indicative of cardiomyopathy (26,27). The mechanism of cardiac dysfunction in the present model is not clearly known. However, previous studies have attributed such an effect to diabetes-induced defects in the exchangers of Na^+/H^+ and Na^+/Ca^{2+} (28), calcium ion metabolism (29) as well as increased blood glucose, oxidative stress (30), or apoptosis in the myocardial cells (31,32). Therefore, we measured serum levels of SOD and GRx, as markers of oxidative stress, and found that they decreased in the present model of simultaneous type 2 diabetes and renal hypertension. Consequently, we might be able to suggest that, in agreement with earlier suggestions (31,32), cardiac dysfunction in the present model might be partly due to increased oxidative stress.

Our findings show that 4 weeks treatment with HEAEL prevented the increase of blood pressure in rats with simultaneous renal hypertension and type 2 diabetes. This finding is similar to our earlier study (17) that this extract reduced the blood pressure in the same model, or those of others that other Allium species such as *A. sativum* and its preparations lowered blood pressure in hypertensive patients (33) and spontaneously hypertensive rats (13). The mechanisms of antihypertensive effects of HEAEL have not been investigated. However, we have shown that it may be related to the enhancement of release of endothelial NO as well as sympathoplegic and antioxidant activities (17). Moreover, the antihypertensive effects of other Allium species such as *A. sativum* have been attributed to the reduction of angiotensin converting enzyme activity (34,35), hyperpolarization of vascular smooth muscle by opening the K^+ channels as well as stimulation of NO synthesis (15). Whether or not such mechanisms are involved in the antihypertensive effects of HEAEL needs to be examined.

The present study represents the first to show that HEAEL offered a cardioprotective effect in rats with simultaneous type 2 diabetes and renal hypertension. This finding is similar to those of reports that other Allium species including *A. ursinum* (36), *A. humile* (23) and *A. sativum* (16,37) were cardioprotective in ischemia and reperfusion (23,36), isoproterenol (16), or doxorubicin (37) - induced myocardial injuries. The possible mechanism of HEAEL cardioprotection is not known. However, previous studies have attributed the cardioprotective effect of Allium species to free radical scavenging activity, reduction of oxidative stress, and preservation of endogenous antioxidant activity (38,39). The present study showed that administration of HEAEL was associated with increased serum levels of SOD and GRx. Therefore, such antioxidant activity may partly explain the HEAEL-induced cardioprotection. How the antioxidant activity of HEAEL led to cardioprotection in the present study is not clear. However, previous studies attributed the cardioprotective effects of antioxidant compounds to reduction of programmed cell death, fibrosis, and contractile dysfunction (40).

The HEAEL-induced cardioprotection may also be partly due to decreased coronary resistance, arterial blood pressure and afterload, and myocardial infarct size. The present study shows that administration of the extract was associated with decreased coronary resistance, and therefore, increased coronary flow. Increased coronary flow might

have increased the delivery of oxygen and nutrients to myocardial cells, and resulted in the improved cardiac performance before ischemia. The HEAEL-induced decrease of infarct size and coronary effluent CK-MB is in agreement with previous studies that other Allium species reduced infarct size or markers of cardiac injury in ischemia reperfusion (23,41), as well as in isoproterenol (16) and doxorubicin- (37)-induced cardiomyopathies.

The present study show that HEAEL decreased FBG in rats with simultaneous renal hypertension and type 2 diabetes. This finding is consistent with our earlier report using the same animal model (17), and with the results reported forother Allium species (11,42,43). Extracts of *A. sativum* (11,12,44) were reported to have antidiabetic effects in rats with streptozotocin-induced diabetes (11,44) and in patients with type 2 diabetes mellitus (12). Such antidiabetic effects were characterized by reduction of blood glucose and hemoglobin A1c, and increased serum insulin levels (11,12,44).

Our findings show that the effects of two doses of the extract were only significantly different for SBP and preischemia (baseline) LVDP. The lack of significant difference in the effects of extract on other parameters might be due to the insufficient doses of the extracts. The doses might have been too close to cause significantly different effects on studied parameters. Alternatively, it may be due to the nature of the measured parameters, which cannot guarantee uniform changes in response to the extract.

CONCLUSION

In conclusion, the findings show that in rats with simultaneous type 2 diabetes and renal hypertension, HEAEL prevented the increase of blood pressure and glucose, and myocardial dysfunction possibly by an antioxidant property.

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