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Basic nutritional investigation

Beneficial effects of argan oil on blood pressure, insulin resistance, and oxidative stress in rat

Adil El Midaoui Ph.D. [a,b,*], Youssef Haddad M.Sc. [a], Réjean Couture Ph.D. [a]

[a] Department of Molecular and Integrative Physiology, Faculty of Medicine, Université de Montréal, Montreal, Quebec, Canada
[b] Department of Biology, FST Errachidia, Moulay Ismail University, Errachidia, Morocco

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ABSTRACT

Objective: The aim of the present study was to investigate whether a 5-wk treatment with argan oil, which is known for its antioxidant properties, can reduce arterial hypertension, hyperglycemia, insulin resistance, and enhanced basal superoxide anion production and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity in the aorta of glucose-fed rats.
Methods: Sprague-Dawley rats had free access to a drinking solution containing 10% D-glucose or tap water (control) for 5 wk. The effect of argan oil in glucose-fed rats was compared with that of corn oil given daily by gavage (5 mL/kg) over a 5-wk period. Oxidative stress was evaluated by measuring the superoxide anion production and the NADPH oxidase activity using the lucigenin method.
Results: The 5-wk treatment with glucose led to increases in systolic blood pressure, plasma glucose, and insulin levels as well as an increase in the insulin resistance index in association with a rise in superoxide anion production and NADPH oxidase activity (sensitive to diphenyleneiodonium) in the aorta. The simultaneous treatment with argan oil prevented or significantly reduced all of these effects, yet the same treatment with corn oil had a positive effect only on hyperinsulinemia and insulin resistance.
Conclusions: The findings from the present study demonstrated that argan oil treatment reduced elevation of blood pressure, hyperglycemia, and insulin resistance through its antioxidative properties in glucose-fed rats. Hence, argan oil, which is now available in the market as a consumable food, may be of potential therapeutic value in the treatment of arterial hypertension and insulin resistance.

Introduction

Diabetes mellitus is recognized as an important cardiovascular risk factor. The association of diabetes to hypertension potentiates the degree of cardiovascular risk, so recent therapeutic guidelines recommend reducing the blood pressure (BP) of hypertensive patients with diabetes to levels below those recommended for other hypertensive patients. Several hypotheses were suggested to explain the enhanced risks associated with diabetes and hypertension (HTN); among these, one of the most plausible is an increase in oxidative stress [1]. Oxidative stress may result from either excessive production of reactive oxygen species (ROS), especially the superoxide anion ($O_2^{\bullet -}$) or from reduced antioxidant reserve. In fact, elevated free radicals have been postulated to participate in the development of complications in insulin resistance (IR), diabetes, and HTN [2–4]. Indeed, one study reported that superoxide anion production and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity in aortic tissue was elevated in hypertensive insulin-resistant rats [5]. Moreover, studies have demonstrated that antioxidant treatment with α-tocopherol (vitamin E) reduces oxidative stress and the increase in BP in spontaneously hypertensive rats (SHR) [6]. Additionally, α-tocopherol was found to reverse the glucose-stimulated

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* Corresponding author. Tel.: +1 514 343 6111; fax: +1 514 412 2111.
E-mail address: adil.el.midaoui@umontreal.ca (A. El Midaoui).

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hyperinsulinemia in obese Zucker rats [7] and to improve insulin action in patients with type 2 diabetes [8].

The relationship between diet and the development of arterial HTN, diabetes, and cardiovascular diseases (CVDs) has been the subject of various studies [9,10]. Investigations have shown that virgin olive oil, which is rich in oleic acid, decreases the incidence of cardiovascular risk factors such as the lipoprotein profile, high BP, and glucose metabolism [11]. Argan oil is another vegetable oil rich in unsaturated fatty acids, principally oleic acid and linoleic acid. Argan oil is produced from the fruits of the argan tree (*Argania spinosa* (L.) Skeels, 1911) that naturally grows in Morocco. Virgin argan oil is obtained by a cold-pressed technique [12] and consequently is not altered during the extraction step [13]. Interestingly, the unsaponifiable fraction of this oil is essentially rich in antioxidant compounds such as tocopherols, which are present in a higher proportion compared with olive oil (637 versus 258 mg/kg, respectively) and particularly in its γ-isoform (75%) [14]. In fact, studies have shown that the decrease in lipid peroxides induced by argan oil consumption was associated with an improvement in antioxidant status in healthy men [15–18]. A 2015 study demonstrated that argan oil reduced the increase in plasma hydroperoxide, thiobarbituric acid-reacting substances, and susceptibility of low-density lipoprotein (LDL) to copper-induced oxidation in high-fat diet-induced obese rats [19]. Additionally, argan oil was found to lower BP and to improve endothelial dysfunction in SHR [20]. Furthermore, investigators have reported that argan oil prevents defects in insulin signaling in both fat and liver of obese insulin-resistant rats [21].

To our knowledge, no study to date has examined the effects of argan oil on two important cardiovascular risk factors conjointly, namely HTN and IR induced by a high-carbohydrate diet. Because argan oil is now available as a consumable food, it is important to elucidate the mechanism by which it can prevent or improve cardiovascular risk factors. Therefore, the present study was designed to investigate whether a chronic 5-wk treatment with argan oil can improve arterial HTN, hyperglycemia, hyperinsulinemia, and IR, and increase basal superoxide anion production and NADPH oxidase activity at the vascular level in hypertensive insulin-resistant rats.

Materials and methods

Animals and procedures

All experimental methods and animal care procedures were approved by the Animal Care Committee of our university (CDEA protocol 14-078), in accordance with the guiding principles as enunciated by the Canadian Council on Animal Care. Male Sprague-Dawley (SD) rats weighing 230 to 250 g (Charles River Laboratories, St-Constant, Qc, Canada) were housed two per cage, under controlled conditions of temperature (22°C) and humidity (43%), on a 12-h light/dark cycle. Four groups of 10 rats were treated for 5 wk as follows: Group 1 had free access to a drinking solution of 10% D-glucose (Sigma-Aldrich, Canada) and to a normal chow diet (Charles River Rodent); group 2 had free access to 10% D-glucose and was treated daily by gavage with argan oil (5 mL/kg); group 3 had free access to 10% D-glucose and was treated daily by gavage with corn oil (5 mL/kg); group 4 represents the control group and had free access to tap water only. In a preliminary study, we found that the daily dose of 3 mL/kg of argan oil had no significant effect on high systolic blood pressure (SBP), whereas the daily dose of 5 mL/kg blunted the increase in BP in 4-wk glucose-fed rats. The dose of argan oil was then selected according to our preliminary study and to a previously published study [22]. Argan oil was obtained from Argan3 Inc (Montreal, QC, Canada) and was 100% pure with the following composition: 14% palmitic acid, 5% stearic acid, 43.5% oleic acid, 37% linoleic acid, 0.6% linolenic acid, sterols, 45% schottenol, 35% spinasterol, and 1034 mg/kg tocopherols with no additives or ingredients. The duration of treatment with argan oil was based on a preliminary study and previous investigations showing that 4 wk of an antioxidant diet treatment notably α-lipoic acid, prevented the development of arterial HTN and IR in glucose-fed rats [23,24]. It is noteworthy that in the present study, the 5-wk treatment with argan oil had no detrimental secondary effects in glucose-fed rats. Corn oil was purchased from ACH Food Companies Inc (Oakville, ON, Canada) and had the following composition: 13% palmitic acid, 3% stearic acid, 31% oleic acid, 52% linoleic acid, and 1% linolenic acid. Corn oil was found to be safe with no clinical signs or toxicity at 5 mL/kg daily for 12 wk in SD treated rats [25].

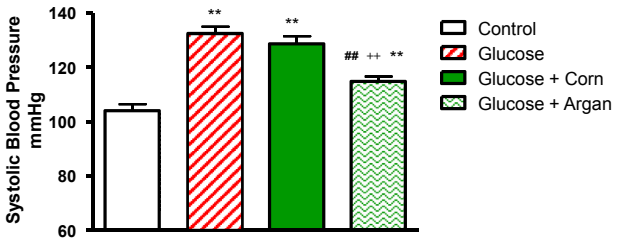

Fig. 1. Effects of 5 wk glucose feeding, with or without corn oil or argan oil treatment, on systolic blood pressure expressed in mm Hg. Values are mean ± SEM of 8 to 10 rats per group. $^{**}P < 0.01$ versus control rats, $^{\#\#}P < 0.01$ versus glucose, $^{\dagger\dagger}P < 0.01$ versus glucose + corn oil.

After 5 wk of treatment, SBP was measured by tail-cuff plethysmography in each group based on an average of five readings per animal (ADI Instruments Inc., Colorado Springs, CO, USA) and registered with the ADI Instruments Program (Lab Chart Pro7.Ink). The rats were sacrificed by decapitation after light anesthesia with isoflurane. The blood was collected in a vacutainer tube early in the morning after fasting overnight (16 h) for plasma insulin determination. The aorta was removed and kept frozen at –20°C until use.

Measurement of metabolic parameters

Blood glucose concentrations in overnight-fasted rats were measured with a glucometer (Accu-Chek Aviva, Roche Diagnostics, Laval, QC, Canada). Plasma insulin levels were determined by radioimmunoassay method (Rat insulin RIA kit, Millipore, St Charles, MO, USA). To evaluate the degree of IR, the homeostasis model assessment (HOMA) was used as an index of IR and calculated by the following formula: insulin (μU/mL) × glucose (mmol/L)/22.5 [26].

Superoxide anion measurement

Superoxide anion production was measured from frozen aortic slices using the lucigenin-enhanced chemiluminescence method as described previously [27,28]. Briefly, small slices from aorta were preincubated in Krebs-Hepes buffer (saturated with 95% O_2 and 5% CO_2, at room temperature) for 30 min and then transferred to a glass scintillation vial containing 5 μmol/L of lucigenin (200 μL/2 mL Krebs-Hepes) for the determination of basal $O_2^{\bullet -}$ levels. The chemiluminescence was recorded every minute for 10 min at room temperature in a liquid scintillation counter (Wallac 1409, Turku, Finland). Lucigenin counts were expressed as cpm/mg of dry weight tissue. Moreover, 0.1 mM NADPH was added to the vials before counting to assess the activation of NADPH oxidase activity in the samples. Basal superoxide-induced luminescence was then subtracted from the luminescence value induced by NADPH [29]. To confirm the involvement of NADPH oxidase, diphenyleneiodonium (DPI, 10 μmol/L), a selective inhibitor of NADPH oxidase was used according to a previous study [30].

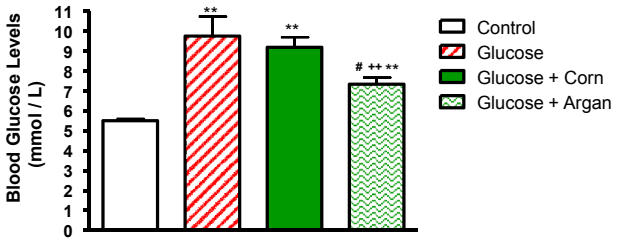

Fig. 2. Effects of 5 wk glucose feeding, with or without corn oil or argan oil treatment, on blood glucose levels expressed in mmol/L. Values are mean ± SEM of 8 to 10 rats per group. $^{**}P < 0.01$ versus control rats; $^{\#}P < 0.05$ versus glucose; $^{\dagger\dagger}P < 0.01$ versus glucose + corn oil.