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Original Research

Watermelon consumption improves inflammation and antioxidant capacity in rats fed an atherogenic diet

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ABSTRACT

Cardiovascular disease (CVD) is the leading cause of death in the United States. Watermelon, rich in antioxidants and other bioactive components, may be a viable method to improve CVD risk factors through reduced oxidative stress. The purpose of the study was to determine the effects of watermelon powder consumption on lipid profiles, antioxidant capacity, and inflammation in dextran sodium sulfate (DSS)–treated rats fed an atherogenic diet. We hypothesized that watermelon would increase antioxidant capacity and reduce blood lipids and inflammation through modulation of related gene expression. Forty male-weanling (21 days old) Sprague-Dawley rats were divided into 4 groups (10 per group, total N = 40) in a 2 diets (control or 0.33% watermelon) × 2 treatments (with or without DSS) factorial design using an atherogenic diet. Watermelon-fed groups exhibited significantly lower serum triglycerides, total cholesterol, and low-density lipoprotein cholesterol ($P < .05$). C-reactive protein levels were significantly lower in watermelon-fed rats than the control ($P = .001$). In addition, oxidative stress as measured by thiobarbituric acid reactive substances was significantly lower in watermelon groups ($P = .001$). Total antioxidant capacity, superoxide dismutase, and catalase activities were greater in watermelon groups ($P < .05$). Aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and lactate dehydrogenase were significantly lower in DSS-treated rats when watermelon was consumed ($P < .05$). Fatty acid synthase, 3-hydroxy-3methyl-glutaryl-CoA reductase, sterol regulatory element-binding protein 1, sterol regulatory element-binding protein 2, and cyclooxygenase-2 gene expression was significantly downregulated in the watermelon group without DSS ($P < .05$). These findings indicate that watermelon improves risk

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; ANOVA, analysis of variance; AST, aspartate aminotransferase; CAT, catalase; COX-2, cyclooxygenase 2; CRP, C-reactive protein; CVD, cardiovascular disease; DSS, dextran sodium sulfate; FAS, fatty acid synthase; GPx, glutathione peroxidase; GST, glutathione S-transferase; HDL, high-density lipoprotein; HMGCR, 3-hydroxy-3methyl-glutaryl-CoA reductase; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; NO, nitric oxide; PCR, polymerase chain reaction; RelA, NF-kappa-B p65 subunit; RNA, ribonucleic acid; SNK, Student-Newman-Keuls; SOD, superoxide dismutase; SREBP-1, sterol regulatory element-binding protein 1; SREBP-2, sterol regulatory element-binding protein 2; TBARS, thiobarbituric acid reactive substances; TC, total cholesterol; TG, triglyceride.

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factors for CVD in rats through better lipid profiles, lower inflammation, and greater antioxidant capacity by altering gene expression for lipid metabolism.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States. Coronary heart disease alone costs the United States more than US $108 billion annually [1]. The high cost of currently treating CVD through pharmaceutical treatments demands the production of a less costly and effective alternative.

Supplementation of L-arginine and L-citrulline has yielded significantly improved levels of total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol [2]. Further, L-arginine supplementation reverses the effects of a high-fat diet by decreasing inflammation and increasing antioxidant status [3,4]. Oral consumption of L-arginine also improves endothelial function by reducing the susceptibility of LDL to oxidation in coronary artery disease patients [5].

It is possible to directly supplement L-arginine; however, this method can cause gastrointestinal discomfort, nausea, and diarrhea, making it unsuitable for daily intake [6]. These adverse side effects may result from quick and excessive production of nitric oxide (NO) by the gastrointestinal tract and from compromised intestinal absorption of additional dietary amino acids [7]. These side effects are not acceptable; thus, alternative dietary and cost-effective means of providing L-arginine and other important nutrients need to be researched. Emerging research is focusing on alternative nutritional regimens to prevent and treat CVD and its associated risk factors. Evidence is growing to support the use of fruit and fruit extracts as a beneficial component for preventing or treating CVD [8,9]. One way to supplement L-arginine is to consume foods that are high in L-arginine or its dietary precursor L-citrulline.

Watermelon (*Citrullus lanatus*) is naturally rich in L-citrulline, varying in amounts from 0.7 to 3.6 mg/g fresh [10], and could possibly produce similar or better effects than L-arginine supplementation. Studies have demonstrated that *C lanatus* juice possesses antioxidant, anti-inflammatory, and antihypertensive properties [11–13]. Watermelon is already known to play an effective role in reducing oxidative stress through the phytochemical lycopene [14]. Watermelon is also high in other antioxidants, which have been linked to decreased risk of coronary heart disease [14]. *Citrullus lanatus* juice supplementation was also shown to raise serum levels of L-arginine and L-citrulline as effectively as elemental supplementation [11,15,16].

Many studies have examined the impacts of individual components of *C lanatus*; however, little has been done to demonstrate the effects of whole watermelon supplementation in powder form on lipid profiles, antioxidant capacity, and inflammation. It remains unclear whether watermelon powder supplementation has the same beneficial effects on serum lipid profiles as elemental supplementation of these bioactive components. The purpose of this study was to determine the effects of L-citrulline–rich watermelon powder supplementation on antioxidant capacity, inflammation, and lipid profiles in dextran sodium sulfate (DSS)–treated rats fed an atherogenic diet. We hypothesized that watermelon powder supplementation would improve multiple risk factors for CVD by promoting positive effects on lipid profiles, antioxidant markers, and inflammation. We used a rodent rat model to allow us to examine the effects of watermelon powder on hepatic expression of genes involved in lipid metabolism.

2. Methods and materials

2.1. Animals and diets

Forty 21-day-old, male Sprague-Dawley rats (59.8 ± 0.9 g; Harlan, Placentia, CA) were housed in wire-bottomed cages individually on a 12-hour light-dark cycle in a research room at San Diego State University. Temperature and humidity were controlled at approximately 20°C to 24°C and 40% to 45%, respectively. Animals were allowed to acclimate to their environment for 2 to 3 days before the start of the study. The procedures and training for use of the animals were conducted and approved by the San Diego State University animal subjects program under the Institutional Animal Care and Use Committee.

Rats were randomly divided into 4 groups of 10, consuming atherogenic diets consisting of 33% sugar by weight, 21% fat by weight, 3% cholesterol by weight, and 0.33% watermelon powder by weight or a kilocalorie equivalent of maltodextrin (Table 1). The watermelon powder consisted of freeze-dried watermelon solids that had been sieved and was originally manufactured by Milne Fruit Products (Prosser, WA) [13]. Casein (Halran, Madison, WI) contains 3.4% of L-arginine; therefore, the control diet contains 6.8 g L-arginine and 0 g L-citrulline per kilogram diet [17]. The watermelon powder contains L-citrulline (1.35 g) and L-arginine (0.65 g) for 3.3 g of the powder. Watermelon diet provides 7.45 g L-arginine and 1.35 g L-citrulline per kilogram watermelon-supplemented diet [13]. Rats received 1 of the 2 experimental diets for 30 days.

Table 1 – Ingredient composition of the diets fed to rats

Ingredient (g/kg)	Control	Watermelon
Cornstarch	121.7	121.7
Sucrose	328.0	328.0
Cellulose	50.0	50.0
Casein	200.0	200.0
Corn oil	50.0	50.0
Dairy butter	160.0	160.0
Cholesterol	30.0	30.0
Salt mix, AIN-93G	35.0	35.0
Vitamin mix, AIN-93G	10.0	10.0
Methionine	3.0	3.0
Sodium cholate	5.0	5.0
Choline chloride	4.0	4.0
Maltodextrin	3.3	0.0
Watermelon powder	0.0	3.3
Total	1000.0	1000.0