Effect of *Hibiscus sabdariffa* Calices on Dyslipidemia in Obese Adolescents: A Triple-masked Randomized Controlled Trial

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ABSTRACT

Objective: We aimed to evaluate the effects of *Hibiscus sabdariffa* (HS) calices on controlling dyslipidemia in obese adolescents. Methodology: In this triple blind randomized placebo-controlled clinical trial which was registered in the Iranian registry for clinical trials (IRCT201109122306N2), 90 obese adolescents aged 12-18 years with documented dyslipidemia were randomly assigned in two groups of cases who received 2 grams of fine powdered calices of *Hibiscus sabdariffa* per day for one month and controls who received placebo powder with the same dietary and physical activity recommendations and duration of exposure. Full lipid profile and fasting blood sugar measured before and after the trial. Data were analyzed using multivariate general linear model. Findings: Overall, 72 participants (mean age of 14.21±1.6, 35 boys) completed the trial. The two arms of the study (cases and controls) were not statistically different in terms of age, gender, weight, body mass index (BMI) and lipid profile before the trial. Serum total cholesterol, low density lipoprotein cholesterol and serum triglyceride showed a significant decrease in cases group but high density lipoprotein cholesterol level was not changed significantly. Conclusion: It is concluded that *Hibiscus sabdariffa* calyces powder may have significant positive effects on lipid profile of adolescents which maybe attributed to its polyphenolic and antioxidant content. Further studies are needed on dose-response and formulation optimization.

Keywords: *Hibiscus sabdariffa* L., Metabolic syndrome, hyperlipidemia, Adolescents

1. INTRODUCTION

Cardiovascular diseases (CVD) are generally believed as a major concern responsible for human mortality while being among the foremost causes of preventable death (1, 2, 3, 4). Atherosclerosis is the major reason of cardiovascular diseases and is an important cause of arterial wall disorder which directly influences large and medium-sized arteries. Different factors contribute to atherosclerosis; but dyslipidemia seems to be an important contributor. Elevated low density lipoprotein cholesterol (LDL) and reduced high density lipoprotein cholesterol (HDL) levels were previously known risk factors for developing atherosclerosis (2, 5, 6).

Obesity, as an important cause of CVDs, is associated with diverse cardiovascular disease risk factors like hypertension, dyslipidemia, escalated insulin levels and finally an increased risk of CVD morbidity and mortality in adulthood (3, 7). Modification of some socioeconomic behavioral habits like smoking, alcohol consumption, dietary patterns and physical activity especially from childhood and adolescence is important and effective measures for the prevention of CVDs (8, 9).

Albeit the clinical emergencies of atherosclerosis are displayed in adulthood, early atherosclerotic changes are apparent in youth studied post-mortem. Thus, effective prevention of atherosclerosis is advised to be started in childhood or adolescence (4, 10, 11, 12, 13).

On the other hand the increasing prevalence of childhood obesity is a worldwide trend and is becoming globally a remarkable public health problem. A decline in physical activity and an increase in amount of calorie intake may be responsible for this increasing incidence. Hence, lifestyle modification and weight control in childhood should be noticed enough to reduce the risk of CVD in adulthood (7, 14, 15, 16, 17).
Statins and fibrates are the most common chemicals used to treat plasma lipid disorders; however concerns about their side effects like elevation of liver enzymes, gastrointestinal symptoms, predisposition to cholelithiasis, rhabdomyolysis, myopathy, renal dysfunction, etc and also lack of general agreement about their use in children and adolescents, have persuaded the scientists to find an appropriate substitution for them (11, 15, 18, 19).

Different studies have showed herbal drugs in treatment of dyslipidemia and prevention of LDL-oxidation thanks to their constituents like dietary fibers, vitamins, flavonoids, estrols, polyphenols, antioxidant compounds, etc as invaluable sources. Although these effects are weaker than chemical drugs, their use in primary stages of dyslipidemia and atherosclerosis seems rational (11, 20, 21).

_Hibiscus sabdariffa_ L. [Roselle] is a plant which belongs to the Malvaceae family and is widely cultivated in the tropical areas like Caribbean, Australia, Brazil, Central America, India, Africa, US and Philippines. This plants is used from times as a traditional medicine due to its effects against kidney stones and urinary bladder stones, and also its antibacterial, antifungal, hypcholesterolemic, anti spasmodic and antihypertensive effects. It is used as a folk medicinal plant in Iran and has been recognized as sour tea (22, 23).

_H. sabdariffa_ L. is rich in polyphenols, anthocyanins, flavonoids that may justify its use in prevention of cardiovascular disorders. According to the antioxidant and antilipid peroxidation actions of _Hibiscus_ extract, it is considered that _Hibiscus_ anthocyanins and pro catechric acid may also have a role in amelioration or prevention of these clinical conditions (24, 25). The aim of this study a study was to evaluate the effect of _Hibiscus sabdariffa_ calices on dyslipidemia in obese adolescents.

2. METHODS

Study design

This randomized triple masked placebo controlled clinical trial was conducted from July 2010 to July 2011 in Isfahan cardiovascular research institute, Isfahan (Iran) and registered in the Iranian registry for clinical trials (IRCT201109122306N2). Ninety (n=90) school-age adolescents (12 to 18 years old) who had at least one of these criteria: a) serum triglyceride more than 90 percentile b) serum total cholesterol more than 90 percentile c) LDL more than 90 percentile d) HDL less than 10 percentile, not using tobacco, no history of alcohol consumption or drug abuse, no history of metabolic diseases like diabetes, thyroid gland dysfunction, nephrotic syndrome, chronic pancreatitis, liver and gall bladder diseases and no drug consuming (which affects lipid profiles like statins and hormonal pills like estrogens, progesterones and oral contraceptives) were screened for inclusion of this clinical conditions (24, 25). The aim of this study a study was to evaluate the effect of _Hibiscus sabdariffa_ calices on dyslipidemia in obese adolescents.

3. RESULTS

The total polyphenolic content of _H. sabdariffa_ L. calyx after triple measurement was equivalent to 16.4 milligram Gallic acid (11, 20, 21).

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Acid per gram. A total of 90 eligible volunteers were recruited for the study and 7 participants from the cases and 11 from the controls group dropped out of the study due to irregular consumption of drugs, changing usual diet or irregular attendance for measuring lipid profiles. Finally 36 people completed the study in each group (Figure 1).

The mean age of the subjects in the cases was 14.17±1.61 years and 14.25±1.59 years in the controls. There were no statistically difference in the mean age (p=0.826), gender (p=0.907), body mass index (p=0.648) and lipid profile between the cases and controls before the study. Demographic data of all participants (age, gender and body mass index) are summarized in Table 1.

The results of the multivariate general linear model analysis of lipid profiles outcomes before and after treatment in cases and controls are shown in Table-2. The data showed a significant decrease in LDL, total cholesterol and triglyceride in cases and no significant decrease in HDL (Table 2). In this study no noticeable decrease in triglyceride, total cholesterol and LDL and no significant decrease in HDL (Table 2). In this study no significant drug side effects was reported except some mild gastrointestinal symptoms (e.g. temporary constipation).

4. DISCUSSION

Considering the increasing need to find effective cholesterol lowering agents and the role of diet in reducing atherosclerosis risk, edible plants are markedly being considered as a resources of anti atherosclerosis agents (30). Recently, many clinical studies proposed dyslipidemia as one of the major risk factors for coronary disease. Preclinical observations demonstrate that hypercholesterolemia aggregates accumulation of oxidized Low-density lipoprotein (Ox-LDL) in the arterial wall, promoting endothelial cell dysfunction and therefore promotion of atherosclerosis (24, 31).

* High Density Lipoprotein, ** Low Density Lipoprotein, ***Paired-Samples T test

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AUTHORS’ CONTRIBUTION
Alireza Ghanadi introduced the idea and Ali Mohammad Sabzebarzadeh designed the project. Roya Kelishadi and Shahin Shirani supervised and helped for the clinical part of the work. Ehsan Ataei prepared the proposal and implemented it under the supervision of aforementioned professors. Rasool Soltani and Shirinsadat Badri proofread the research proposal and finalized it. All authors contributed in data analysis, manuscript preparation and read and approved the final manuscript.

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