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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).

Various chemical and herbal types of medications are used nowadays for the prevention and treatment of hyperlipidemia

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, rhabdomyelosis, 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, hypocholesterolemic, antispasmodic 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 procatechuic 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, progestrones and oral contraceptives) were screened for inclusion in the study. Exclusion criteria were lack of patients' compliance with drug regimens at least for one week, pregnancy and lactation, drug sensitivity, presence of any disease which could interact with lipid profiles and need to take of any kind of drugs or other compounds which affects lipid profile like corticosteroids, androgens, estrogenes, progestines, thiazides, beta blockers and thyroid hormones . The study was approved by the institutional ethics committee of Isfahan Medical University of sciences and all participants and their parents or guardians read and signed a written informed consent form before participation (26, 27, 28).

Sample size was determined according the t-student formula. Accordingly the most important variable in this study was considered as serum level of cholesterol which is a quantitative continuous variable and to detect at least 10 mg/dl decrease of this variable in case group (comparing to the controls), with 80% power and 5% type 1 error, suitable sample size was calculated 35 people in each group. To rectify anticipating losses of patients in terminating treatment period, sample size was expanded by 20%. The participants divided into two groups of case and control using table of random numbers.

A registered dietitian explained the same protocols for physical activity and food regimen for both groups. Lipid parameters, fasting blood sugar and thyroid hormone measured before study to screen for eligible participants for the study. Patients took 6 grams of powders per day (placebo or drug in identical packages) in divided doses for a complete 4 weeks period and the adherence to the therapy were checked after two weeks in the middle of study period for each patient separately. All lipid profile indicators and anthropometric factors were measured after the study period as well.

Collection and preparation of blood samples

All fasting blood samples were taken in the morning between 7:00 and 9:00 am. Venous blood samples obtained after eight hours of fasting and blood samples were frozen for a maximum of two weeks and stored at -70 C° until the time of biochemical analysis. Serum cholesterol levels were measured by enzymatic colorimetric methods using commercial kits obtained from Parsazmoon (Karaj, Iran).

Preparing the dosage form

H. sabdariffa L. was bought from Isfahan (Iran) medicinal plant market and air dried *H. sabdariffa* L. calices were blended into fine powder and then packaged into 2 gram sachets.

Polyphenol content of plant determined using folin-ciocalteu method. 1 gram of powder was added to 100 ml water and refluxed until water boiled. Then the extract was filtered and 1ml of that was diluted with distilled water to 100 ml. Thereafter 20 µl of this solution poured into a test tube and 1.58 ml water and100 ml folin-ciocalteu reagent added and mixed for 5 minutes and then 300 ml of super-saturated sodium bicarbonate solution added. After two hours in room temperature, mixture absorbance measured in 765 nm using a spectrophotometer (Jenway 6105, Staffordshire, UK). A standard curve of Gallic acid was prepared as well (29).

Statistical analysis

The data are presented as Mean ± SD. A Kolmogrov-smirnov test was performed to show normal distribution of all measured data. An independent t-test analysis was performed to verify whether significant differences existed between the anthropometric and biochemical parameters of the subjects in the cases and controls groups at the baseline. Chi-square test used to compare gender variable in cases and controls groups. The paired samples t-test was used to compare differences between subjects of each group before and after the study. A multivariate general linear model test was performed to assess the changes over the time in the anthropometric and biochemical parameters between the two groups and also to offset the effect of confounding factors like age, gender and body mass index (BMI). The level of significance was considered as 0.05.

3. RESULTS

The total polyphenolic content of *H. sabdariffa* L. calyx after triple measurement was equivalent to 16.4 milligram Gallic

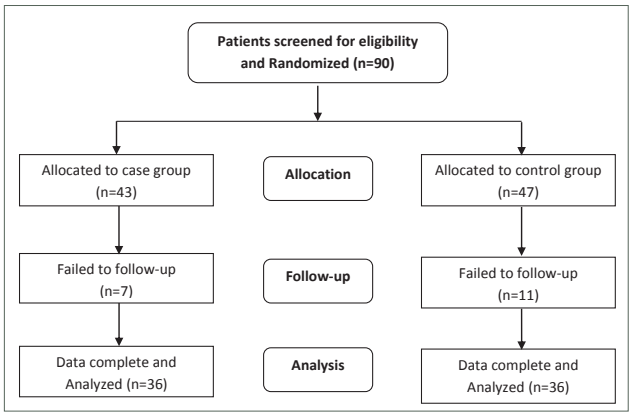

Figure 1. Patient allocation, follow-up and data analysis diagram of the study

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.

Groups	Number of patients (n)	Gender		Average age (years ± SD)	Body Mass Index
		Boys	Girls		
Cases	36	19	17	14.17±1.61	25.66
Controls	36	16	20	14.25±1.59	25.11

Table 1. Demographic data of the study patients

Lipid profile 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 (without any significant decrease in HDL). The p value results of the multivariate general linear model analysis of lipid profiles for triglyceride, total cholesterol, LDL and HDL were 0.01, 0.032, 0.005 and 0.782 respectively. This information reveals 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).

Groups		Cholesterol (mg/dl)	Triglyceride (mg/dl)	LDL** (mg/dl)	HDL* (mg/dl)
Cases	before	186.5±30.42	146±49.87	111.36±24.54	45.64±8.59
	After	176.11±23.1	134.22±50.17	103.36±21.94	43.17±7.77
Controls	before	200.6±43.59	166.17±44.42	125.28±37.75	41.58±9.77
	After	198.5±43.12	163.44±43.64	124.17±36.76	42.17±9.52
Statistical analysis***	Case	P=0.003	P=0.022	P<001	P=0.057
	control	P=0.1	P=0.052	P=0.097	P=0.649

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

Table 2. Lipid profile data of study patients before and after consuming 2 grams of fine powder of H. sabdariffa calices

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).

H. sabdariffa L., an annual herbaceous shrub, is a traditional chinese rose tea, cultivated in tropical areas like Africa, Asia and Central America used effectively in folk medicine. The chemical constituents reported in this plant are phenolic compounds, anthocyanins, flavonoids, protocatechuic acid, Vitamin C and carotenoid (23, 24, 32, 33). Different studies have showed variety of pharmacologic actions of this plant like antioxidative, antimutagenic, anticancer, hypolipidemic and liver protective (24, 32, 34-36). Some studies on the cholesterol lowering effect of *H. sabdariffa* L. have previously been conducted on animals and humans (24, 37, 38).

In a study conducted to establish the effect of anthocyanins content of *H. sabdariffa* L., it was observed that extracts of *Hibiscus* flowers prevents LDL oxidation and macrophage death (39). Another investigation about effects of *H. sabdariffa* L. extract powder and preventive diet in patients with metabolic syndrome showed antihypertensive and antihyperlipidemic impacts for this plant (40). Another study revealed that the aqueous extract of *H. sabdariffa* L. calices modulates the production of monocyte chemoattractant protein-1 in humans and lower production of mcp1, which means the slower development of atherosclerosis (41, 42). Also another study proved the effect of anthocyanin extracted from *Hibiscus* in attenuating oxidized LDL-mediated foam cell formation involving regulation of CD36 gene (43).

According to statistical data in cases and controls before and after consumption of *H.s sabdariffa* L. powder and placebo, the results show that using up the plant for one month decreases serum total cholesterol, triglyceride and LDL effectively. Meanwhile, LDL downturn (p=0.005) by 7% fall and triglyceride downward trend (P=0.01) by 9% fall show more prominent decline in comparison with other parameters; hence it shows the noticeable capacity of this herbal plant in modifying serum LDL and triglyceride. The short period of drug usage (a one month period) may justify the ineffectiveness of the plant on HDL, and longer exposures to the drug may be needed to have a more accurate conclusion.

5. CONCLUSION

It is concluded that *H. sabdariffa* L. due to its polyphenolic and antioxidant compounds may have positive effects on serum lipids profile and presumably can be considered for future studies on prevention and treatment of dyslipidemia and atherosclerotic disorders in adolescents.

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AUTHORS'CONTRIBUTION

Alireza Ghannadi introduced the idea and Ali Mohammad Sabzghabaee designed the study. 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.

REFERENCES

1. Labarthe D. Epidemiology and Prevention of Cardiovascular Diseases: A Global Challenge. 2nd ed: Jones and Bartlett Publishers, 2011.
2. Tsompanidi EM, Brinkmeier MS, Fotiadou EH, Giakoumi SM, Kypreos KE. HDL biogenesis and functions: role of HDL quality and quantity in atherosclerosis. Atherosclerosis. 2010; 208(1): 3-9.
3. He L, Tang X, Song Y, Li N, Li J, Zhang Z, et al. Prevalence of cardiovascular disease and risk factors in a rural district of Beijing, China: a population-based survey of 58,308 residents. BMC Public Health.12: 34.
4. May AL, Kuklina EV, Yoon PW. Prevalence of Cardiovascular Disease Risk Factors Among US Adolescents, 1999-2008. Pediatrics. 2012; 129(6): 1035-1041.
5. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, et al. Heart disease and stroke statistics–2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009; 119(3): 480-486.
6. Stepien E, Kablak-Ziembicka A, Musialek P, Tylko G, Przewlocki T. Fibrinogen and carotid intima media thickness determine fibrin density in different atherosclerosis extents. International Journal of Cardiology. 2012; 157(3): 411-413.
7. Kim HM, Park J, Kim HS, Kim DH, Park SH. Obesity and cardiovascular risk factors in Korean children and adolescents aged 10-18 years from the Korean National Health and Nutrition Examination Survey, 1998 and 2001. Am J Epidemiol. 2006; 164(8): 787-793.
8. Music S, Milanovic, Ivicevic A, Uhernik, Dzakula A, Brborovic O, et al. The CroHort Study: cardiovascular behavioral risk factors in adults, school children and adolescents, hospitalized coronary heart disease patients, and cardio rehabilitation groups in Croatia. Antropol. 2012; 36: 265-268.
9. Padwal RS, Sharma AM. Prevention of cardiovascular disease: Obesity, diabetes and the metabolic syndrome. Cardiol. 2010; 26: 18-20.
10. Morrison KM, Dyal L, Conner W, Helden E, Newkirk L, Yusuf S, et al. Cardiovascular risk factors and non-invasive assessment of subclinical atherosclerosis in youth. Atherosclerosis. 2010; 208(2): 501-505.
11. Kalra S, Gandhi A, Kalra B, Agrawal N. Management of dyslipidemia in children. Diabetol Metab Syndr. 2009; 1(1): 26.
12. Descamps OS, Tenoutasse S, Stephenne X, Gies I, Beauloye V, Lebrethon MC, et al. Management of familial hypercholesterolemia in children and young adults: Consensus paper developed by a panel of lipidologists, cardiologists, paediatricians, nutritionists, gastroenterologists, general practitioners and a patient organization. Atherosclerosis. 2011; 218(2): 272-280.
13. Strong JP, Malcom GT, McMahan CA, Tracy RE, Newman WP, 3rd, Herderick EE, et al. Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. JAMA. 1999; 281(8): 727-735.
14. Gupta N, Goel K, Shah P, Misra A. Childhood Obesity in Developing Countries: Epidemiology, Determinants, and Prevention. Endocr Rev. 2011.
15. O'Gorman CS, O'Neill MB, Conwell LS. Considering statins for cholesterol-reduction in children if lifestyle and diet changes do not improve their health: a review of the risks and benefits. Vasc Health Risk Manag. 2010; 7: 1-14.
16. Raj M. Obesity and cardiovascular risks in children and adolescents. Indian journal of endocrinology and metabolism. 2012; 16(1): 13-19.
17. Junior IFF, Monteiro PA, Silveira LS, Cayres SU, Antunes BM, Bastos KN, et al. Resting heart rate as predictor of metabolic dysfunctions in obese children and adolescents. BMC Pediatrics. 2012; 12(5): 1-22.
18. Jain KS, et al. The biology and chemistry of hyperlipidemia. Bioorg Med Chem. 2007; 15(14): 4674-499.
19. Michos ED, Sibley CT, Baer JT, Blaha MJ, Blumenthal RS. Niacin and Statin Combination Therapy for Atherosclerosis Regression and Prevention of Cardiovascular Disease Events: Reconciling the AIM-HIGH (Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides: Impact on Global Health Outcomes) Trial With Previous Surrogate Endpoint Trials. Journal of the American College of Cardiology. 2012; 59(23): 2058-2064.
20. Hasani-Ranjbar S, Nayebi N, Moradi L, Mehri A, Larijani B, Abdollahi M. The efficacy and safety of herbal medicines used in the treatment of hyperlipidemia; a systematic review. Curr Pharm Des. 2010; 16(26): 2935-2947.
21. Singh PK, Baxi DB, Mukherjee R, Ramachandran AV. Evaluation on the efficacy of polyherbal supplement along with exercise in alleviating dyslipidemia, oxidative stress and hepatic and renal toxicity associated with type-1 diabetes. Herbal Medicine and Toxicology. 2010; 4(2): 35-43.
22. Mozaffari-Khosravi H, Jalali B, Afkhami-Ardakani M. Effect of Sour Tea (Hibiscus Sabdariffa) on Blood Glucose, Lipid Profile and Lipoproteins in Diabetics. Iranian Journal of Endocrinology and Metabolism. [Original]. 2009; 10(6): 589-597.
23. Mahadevan N, Shivali, Kamboj P. Hibiscus sabdariffa Linn.- an overview. Natural product radiance. 2008; 8(1): 77-83.
24. Lin TL, Lin HH, Chen CC, Lin MC, Chou MC, Wang CJ. Hibiscus sabdariffa extract reduces serum cholesterol in men and women. Nutrition Research. 2007; 27(3): 140-145.
25. Ali BH, Wabel NA, Blunden G. Phytochemical, Pharmacological and Toxicological Aspects of Hibiscus sabdariffa L. A Review. Phytotherapy research. 2005; 19: 369-375.
26. Cubeddu LX, Cubeddu RJ, Heimowitz T, Restrepo B, Lamas GA, Weinberg GB. Comparative lipid-lowering effects of policosanol and atorvastatin: a randomized, parallel, double-blind, placebo-controlled trial. Am Heart J. 2006; 152(5): 982 e1-5.
27. Kliegman RM, Stanton B, Geme JS, Schor N, Behrman RE. Nelson Textbook of Pediatrics: Expert Consult Premium Edition–Enhanced Online Features and Print: Elsevier–Health Sciences Division, 2004.
28. Shidfar F, Homayounfar R, Fereshtehnejad SM, Kalani A. Effect of folate supplementation on serum homocysteine and plasma total antioxidant capacity in hypercholesterolemic adults under lovastatin treatment: a double-blind randomized controlled clinical trial. Arch Med Res. 2009; 40(5): 380-386.
29. Waterman P, Mole S. Analysis of Phenolic Plant Metabolites. Blackwell Scientific Publication. 1994: 83-85.
30. Fraczek M, Szumilo J, Podlodowska J, Burdan F. [Resveratrol—phytophenol with wide activity]. Pol Merkur Lekarski. 2012; 32(188): 143-146.
31. Hirunpanich V, Utaipat A, Morales NP, Bunyapraphatsara N, Sato H, Herunsale A, et al. Hypocholesterolemic and antioxidant effects of aqueous extracts from the dried calyx of Hibiscus sabdariffa L. in hypercholesterolemic rats. Journal of Ethnopharmacology. 2006; 103(2): 252-260.
32. Kuriyan R, Kumar DR, R R, Kurpad AV. An evaluation of the hypolipidemic effect of an extract of Hibiscus Sabdariffa leaves in hyperlipidemic Indians: a double blind, placebo controlled trial. BMC Complement Altern Med. 2010; 10: 27.
33. Carvajal-Zarrabal O, Waliszewski S, Barradas-Dermitz D, Orta-Flores Z, Hayward-Jones P, Nolasco-Hipólito C, et al. The consumption of Hibiscus sabdariffa dried calyx ethanolic extract reduced lipid profile in rats. plant foods Hum nutr. 2005; 60(4): 153-159.
34. Mohd-Esa N, Hern FS, Ismail A, Yee CL. Antioxidant activity in different parts of roselle (Hibiscus sabdariffa L.) extracts and potential exploitation of the seeds. Food Chemistry. 2010; 122(4): 1055-1060.
35. Perez-Torres I, Ruiz-Ramirez A, Banos G, El-Hafidi M. Hibiscus Sabdariffa Linnaeus (Malvaceae), curcumin and resveratrol as alternative medicinal agents against metabolic syndrome. Cardiovasc Hematol Agents Med Chem. 2012.
36. Gurrola-Diaz CM, Garcia-Lopez PM, Sanchez-Enriquez S, Troyo-Sanroman R, Andrade-Gonzalez I, Gomez-Leyva JF. Effects of Hibiscus sabdariffa extract powder and preventive treatment (diet) on the lipid profiles of patients with metabolic syndrome (MeSy). Phytomedicine. 2010; 17(7): 500-505.
37. Chen C, Hsu J, Wang S, Chiang H, Yang M, Kao E, et al. Hibiscus sabdariffa extract inhibits the development of atherosclerosis in cholesterol-fed rabbits. Agric Food. 2003; 51: 5472-5477.
38. Chen C, Chou F, Ho Y, Lin W, Wang C, Hao E, et al. Inhibitory effects of Hibiscus sabdariffa L., extract on low density lipoprotein oxidation and anti-hyperlipidemia in fructose-fed and cholesterol fed rats. Sci Food Agric. 2004; 84: 1989-1996.
39. Chang YC, Huang KX, Huang AC, Ho YC, Wang CJ. Hibiscus anthocyanins-rich extract inhibited LDL oxidation and oxLDL-mediated macrophages apoptosis. Food and Chemical Toxicology. 2006; 44(7): 1015-1023.
40. Gurrola-Diaz CM, Garcia-Lopez PM, Sanchez-Enriquez S, Troyo-Sanroman R, Andrade-Gonzalez I, Gomez-Leyva JF. Effects of Hibiscus sabdariffa extract powder and preventive treatment (diet) on the lipid profiles of patients with metabolic syndrome (MeSy). Phytomedicine. 2009; 17(7): 500-505.
41. Beltran-Debon R, Alonso-Villaverde C, Aragones G, Rodriguez-Medina I, Rull A, Micol V, et al. The aqueous extract of Hibiscus sabdariffa calices modulates the production of monocyte chemoattractant protein-1 in humans. Phytomedicine. 2010; 17(3-4): 186-191.
42. Stork S, Baumann K, von Schacky C, Angerer P. The effect of 17 beta-estradiol on MCP-1 serum levels in postmenopausal women. Cardiovasc Res. 2002; 53(3): 642-649.
43. Kao ES, Tseng TH, Lee HJ, Chan KC, Wang CJ. Anthocyanin extracted from Hibiscus attenuate oxidized LDL-mediated foam cell formation involving regulation of CD36 gene. Chemico-Biological Interactions. 2009; 179(2-3): 212-218.