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The Effect of Hydroalcoholic Extract of Senna (Cassia Angustifolia Vahl.) on Lipid Profiles in Hyperlipidemic Rats

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ABSTRACT

Background: Abnormality in metabolism of lipids and hyperlipidemia is a risk factor for atherosclerosis which is the major cause of cardiovascular diseases (CVDs). Several herbal drugs are used for the treatment of dyslipidemia. The present study investigates the effects of hydroalcoholic extracts of Senna extract on serum lipid profile among hyperlipidemic rats. **Methods:** Forty eight male Wistar rats were randomly divided into 6 groups of 8 animals, including group 1) normal pellet diet (control), group 2) high fat diet (HFD), group, 3) HFD with 100 mg/kg Senna extract treatment, group 4) HFD with 200 mg/kg Senna extract treatment, group 5) 100 mg/kg pure Senna extract, and group 6) 200 mg/kg pure Senna extract. All the dietary regimens and Senna extract treatments were continued for 30 days. At the end of the experiment, blood samples collected from heart of rats and the lipid profile levels were measured. **Results:** The results indicated that short-term treatment by hydroalcoholic of Senna extract produced a significant reduction in the level of cholesterol, triglyceride, and LDL-C ($P < 0.05$), as well as an increase in HDL-C. The body weight in the HFD group was significantly higher than the other groups ($P < 0.05$). **Conclusion:** Prescription of hydroalcoholic extracts of Senna is effective in the treatment of hyperlipidemia, and can inhibit the weight gain induced by HFD in rats. Some of these effects could be attributed to antioxidants activities, biological and pharmaceutical properties and other protective properties of the Senna extract requiring further investigations.

Keywords: *Senna extract; Hyperlipidemia; Rat*

Introduction

Consumption of a high fat diet (HFD) causes increased lipid accumulation and contributes to various metabolic diseases, such as obesity, hyperlipidemia, atherosclerosis, cardiovascular disease, type 2 diabetes mellitus, and nonalcoholic fatty liver disease (NAFLD) (Bharathi *et al.*, 2018, Hashem and Alazouny, 2016, Soleimani *et al.*, 2016, Zawawi and Ismail, 2018).

Cardiovascular diseases (CVDs) are considered the leading cause of death worldwide, and rapid epidemiological transmission of these diseases has been shown over the past two decades (Ho *et al.*,

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2018). Obesity, lack of physical activity, smoking, and abnormal lipid profile have been recognized as the major risk factors for CVDs (Mozaffarian *et al.*, 2016). The main cause of CVDs is atherosclerosis, which is due to the etiologic and pathologic factors that contribute to the increase in blood lipids (Carr *et al.*, 2019). Low density lipoprotein (LDL-C) is the major atherogenic lipoprotein particle in the circulation, and LDL-C is a key risk factor for CVDs. On the other hand, it has been reported that there is a reverse relationship between serum high density lipoprotein (HDL-C) and CVDs (Kosmas *et al.*, 2018). Abnormality in metabolism of lipids has a main role in atherosclerosis and Chronic Heart Disease (CHD).

Currently, several chemical drugs, such as lovastatin, cholestyramine, and clofibrate are used for the treatment of dyslipidemia. Although the consumption of these drugs may improve dyslipidemia, these drugs are associated with numerous side effects, such as the occurrence of myopathy, rhabdomyolysis, hepatic disorders, muscle tenderness, and digestive problems (Mathur and Kusum Devi, 2016). To improve the lipid profile and blood pressure, dietary modifications are safer and more cost-effective than medical strategies (Kafeshani *et al.*, 2015, Khosravi-Boroujeni *et al.*, 2013, Sahebkar *et al.*, 2016). Several studies have revealed that the consumption of natural substitutes are therapeutically effective, while they have fewer side effects (Hasani-Ranjbar *et al.*, 2010, Wharton *et al.*, 2020).

It is extensively accepted that compliance to a heathier diet leads to positive health outcomes, but recent evidence has shown that nutraceutical compounds have been more widely employed for the adjuvant treatment of dyslipidemia due to their attributed phytotherapic properties, deemed as safe and useful (Ghorbani, 2013, Guo *et al.*, 2014). Medicinal plants are important sources of biologically active natural products which due to their curative properties have been studied for many years (Ahmed *et al.*, 2015, Ahmed *et al.*, 2014). Antioxidant activities of herbal medicines are active in decreasing the toxicities of other medications (Karimi *et al.*, 2015).

Senna *(Cassia angustifolia Vahl.*) is a traditional therapeutic plant belong to the family of Caesalpiniaceae and has been emerged from Saudi Arabia, Egypt, and Yemen (Ahmed *et al.*, 2016). It is full of antioxidant and is known to have strong antioxidant activity. It has many biological and pharmaceutical properties, such as antidiabetic, anti-hyperlipidemic, anticancer, and anti-inflammatory ones. Previous studies have shown that flavonoids are one of Senna effective compounds in the prevention or treatment of antihyperlipidemic (Jani and Goswami, 2019, Raut and Karuppayil, 2014). On this basis, the aim of the current study is to investigate the effects of hydroalcoholic extracts of Senna on levels of lipid profile among hyperlipidemic rats.

Materials and Methods

Animal experiments: The current study was conducted on 48 adult male Wistar rats (body weight 200-220 g). The animals were housed in separate cages (2 rats per cage), under the controlled condition of temperature (22 ± 2 °C), humidity (15-20%), and 12:12 h dark/light cycle with free access to food and water *adlibitum*. The inclusion criteria included male rats and no disease, and the exclusion criteria were as follows: underweight, disease, and bleeding.

Animals were divided into six groups including 1) Normal pellet diet (control), 2) HFD, 3) HFD with 100 mg/kg Senna extract treatment (HFD+100), 4) HFD with 200 mg/kg Senna extract treatment (HFD+200), 5) 100 mg/kg Senna extract (100 mg Ex), and 6) 200 mg/kg Senna extract (200 mg Ex). Each group comprised of eight animals. All the dietary regimens and Senna extract treatments (the alcoholic extract of Senna oral emulsion through gavage over 30 day) were continued for 30 days. The rats were weighed at the beginning and end of the study by digital scales.

Preparation of HFD: In order to provide an HFD, 20 g of pure cholesterol (Sigma corp.) solved in 5 ml olive oil were added to usual pallet diet (1 kg of normal rat diet) for rats (Zarei *et al.*, 2013).

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Afterwards, the mixture was kept under suitable condition in different portions as the rats' food. The base chow (3.05 kcal/g digestible energy) contained 23.1% protein, 64.4% carbohydrate, 4.8% fat (soybean oil), 0.3% vitamins, and 7.7% minerals (Behparvar Company, Tehran, Iran).

Preparation of Cassia angustifolia Vahl extract: For preparation of the alcoholic extract of *Cassia angustifolia Vahl*, Standard methods of extraction were utilized. *Cassia angustifolia Vahl was* cleaned, dried, powdered, and eventually poured into a covered glass container and was mixed with ethanol alcohol 97%. The mixture was permitted to mix well for 72 hours. After that, it was first filtered and then centrifuged. The resultant mixture was placed in a warm bath to allow the complete evaporation of its alcohol (Zarei *et al.*, 2013).

Biochemical analysis: On the final day, the blood samples collected from heart of rats, and total cholesterol (TC), triglyceride (TG), and HDL-C serum levels were measured by commercial kits (Pars Azmoon, Tehran, Iran). LDL-C was calculated according to the Friedewald formula (Friedewald *et al.*, 1972).

Ethical considerations: The experimental protocols were approved by the ethical committee of Zahedan University of Medical Sciences, Iran (IR.ZAUMS.REC.2018.340).

Data analysis: Statistical analysis was performed with SPSS 16.0 using one-way ANOVA followed by the Tukey post hoc test. The results were expressed as Mean ± SEM, and P-value < 0.05 was significantly considered.

Results

The mean weight of the rats in the six groups was not significantly different at the beginning of the study ($P > 0.05$) (**Figure 1**). At the end of study, the mean weight of the HFD group was significantly higher than control group ($P < 0.001$). However, the consumption of *Senna* extract, especially in HFD+200 group led a significant reduction in body weight ($P < 0.01$). Moreover, body weight significantly decreased in the 100 mg and 200 mg extract groups compared to HFD group ($P < 0.01$).

The mean cholesterol level showed a significant difference between the studied groups. A significant increase was observed in cholesterol in the HFD group compared to the control group (**Figure 2**). However, consumption of *Cassia angustifolia Vahl* extract, except for HFD+100 group ($P > 0.05$), significantly reduced the cholesterol level among hyperlipidemic rats ($P < 0.05$).

The mean triglyceride level had a significant increase in HFD group compared to the control group (**Figure 3**). Also, the administration of *Senna* extract significantly decreased the amount of triglyceride (especially in 200 extract group) ($P < 0.05$).

The mean LDL-C level indicated that the consumption of HFD caused a significant increase in LDL-C level compared to the control group ($P < 0.05$, **Figure 4**). The consumption of *Senna* extract can significantly decrease LDL-C level in hyperlipidemic animals ($P < 0.05$).

It was observed that the HDL-C levels in the HFD group were lower than the control group. There was an increase in HDL-C level in rats consuming Senna extract compared to HFD group, but this difference was not significant ($P > 0.05$, **Figure 5**).

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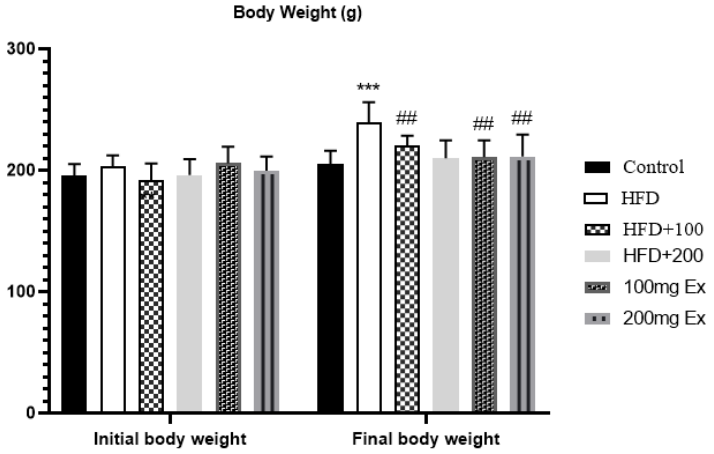

Figure 1. Effect of *Cassia angustifolia Vahl* on body weight, *** p < 0.001 versus control group, ##p < 0.01 versus HFD group.

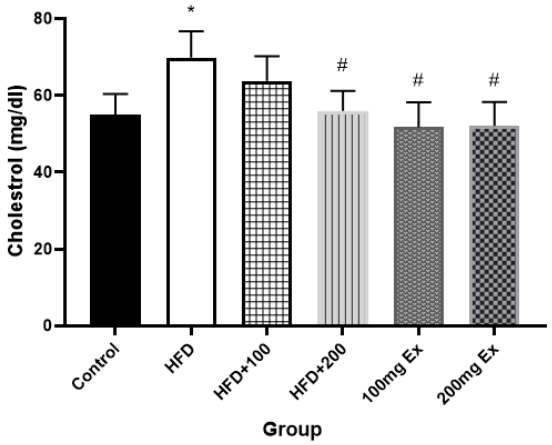

Figure 2. Effect of *Cassia angustifolia Vahl* on cholesterol level, * p < 0.05 versus control group, # p < 0.05 versus HFD group.

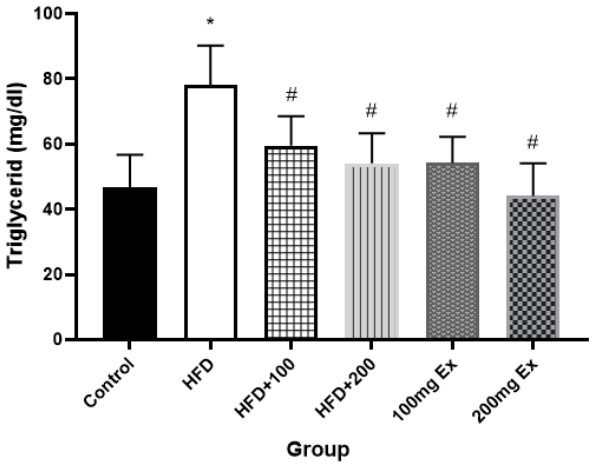

Figure 3. Effect of *Cassia angustifolia Vahl* on TG level, * p < 0.05 versus control group, # p < 0.05 versus HFD group.

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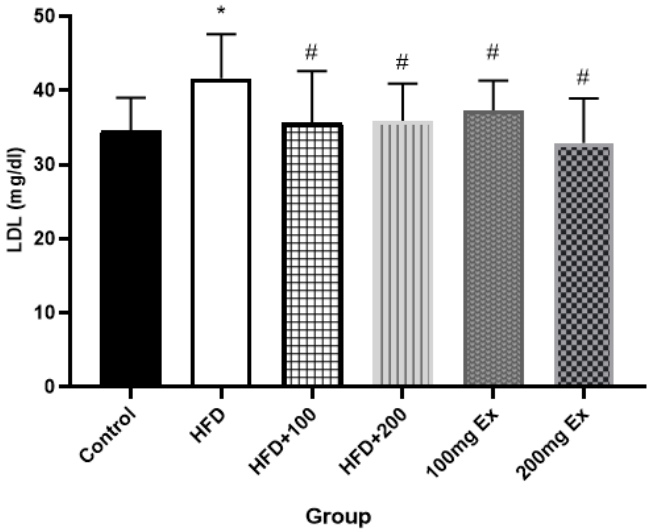

Figure 4. Effect of *Cassia angustifolia Vahl* on LDL-C level, * $p < 0.05$ versus control group, # $p < 0.05$ versus HFD group.

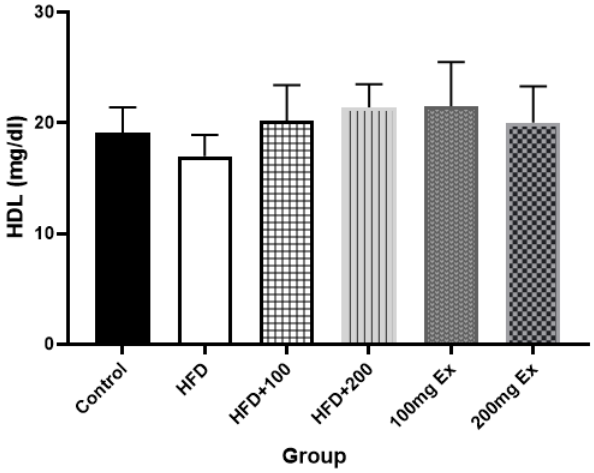

Figure 5. Effect of *Senna extract* on HDL-C level in the studied groups.

Discussion

The results of the present study showed that HFD consumption increases TC, TG, and LDL-C and decreases HDL-C levels. Administration of Senna extract with HFD prevents changes in fat profiles, which indicates its preventive effects. On the other hand, administration of Senna extract alone improves fat profiles more effectively. The study by Gadanya and Muhammad expressed that the use of aqueous extract of Senna reduces the levels of TC, TG, and LDL-C, which is consistent with the results obtained in the present study (Gadanya and Muhammad, 2018). The results of a study by Nanumala *et al.* showed that the use of Senna extract significantly reduces the level of blood lipids in Triton 100 X-induced hyperlipidemia (Nanumala *et al.*, 2014).

Although several studies have shown the beneficial effect of Senna in treating hyperlipidemia (Gupta *et al.*, 2011, Habtemariam, 2013), the antihyperlipidemic principles of Senna have not been identified.

Senna is one of the medicinal plants that has a long history of use in traditional medicine and in recent years is also available as an industrial product and as a laxative. Mucilage is one of the compounds in Senna. These compounds are water-soluble substances that swell and bulk by

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absorbing large volumes of water and form a protective layer on the gastric and intestinal membranes. It has been also mentioned that mucilages reduce cholesterol and blood sugar levels. In the present study, treatment of hyperlipidemic animals with 200 mg/kg of hydroalcoholic extracts of *Senna* produced a significant decrease in total cholesterol, triglyceride, and LDL-C. This is in line with the previous studies (Ayinla *et al.*, 2011, Maryam *et al.*, 2015, Nirmala *et al.*, 2008). It seems that the hypolipidemic effect of *Senna Cassia angustifolia* can be due to the presence of some phytochemical compounds, including alkaloids, flavonoids, and saponins in the Senna extract (Ayinla *et al.*, 2011). All these compounds, especially alkaloids, are known to reduce serum lipid level in animals. In general, herbs used in traditional medicine and their compounds, including dietary fiber, vitamins, flavonoids, sterols, and other antioxidant compounds can play a role in inhibiting LDL-C oxidation and free radical scavenging. It also improves the body's metabolic disorders by affecting the immune system. Flavonoids effect on lipid metabolism in the body reduces the activity of HMG-CoA reductase in the liver. It is also observed that, flavonoids can inhibit LDL-C oxidation by several mechanisms, including 1) scavenging of free radicals; 2) chelating of metal ions and reducing the metals capacity to generate free radicals; 3) sparing of vitamin E and carotenoids in the LDL-C particle, thus protecting LDL-C from oxidation, and this will reduce the risk of CVD (Fuhrman and Aviram, 2001).

The consumption of HFD in rats reduced HDL-C levels compared to the control group. However, this decrease was not statistically significant and intake of the extract had no effect on serum HDL-C levels in the groups. On the other hand, the results of the present study showed that HFD increased blood LDL-C levels in rats, and the appearance of Senna leaf extract in a dose-dependent manner significantly reduced blood LDL-C levels. However, the administration of this extract in groups receiving normal diet had an effect on blood LDL-C levels. Dyslipidemia is a chronic disease caused by metabolic disorders and various factors.

The data also showed that the body weight in the HFD group was significantly higher than the other groups, which may be due to the high calorie intake in this group. The HFD can reflect that calorie intake was high compared to the control group.

Regarding the suggestion that increased food intake enhances serum lipid profile, and according to the results of the study by Jani *et al.*, Senna extract has a significant role in reducing body weight of animals (Jani and Goswami, 2019). Hypercholesterolemia as the main risk factor for atherosclerosis and atherosclerosis is the major cause of heart diseases and stroke. The results indicated that the hydroalcoholic extract of Senna herbal, in addition to having considerable hypolipidemic effects in HFD rats, can lead to weight loss. It is worth mentioning that due to the limited cost and space for keeping rats, the sample size was estimated based on facilities and statistical methods.

Conclusion

Prescription of hydroalcoholic extracts of Senna is effective in the treatment of hyperlipidemia and it also can inhibit the weight gain induced by HFD in rats. It was observed that it increases triglyceride, cholesterol, LDL-C, and decreases HDL-C concentrations due to intake of HFD. Nevertheless, further studies are required to determine the mechanism of these effects. Some of these advantages could be attributed to antioxidants activities, biological and pharmaceutical properties, and other protective properties of Senna extract.

Authors' contributions

Karajibani M contributed and design of research, drafted and final revised the manuscript; Eslahi H, Yarmand S, Miri M, and Naghizadeh M performed experiments and prepared tools and facilities for field study; Montazerifar F performed statically analysis, drafted and final revised the manuscript. All authors read and approved the final draft of manuscript.

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Conflict of interests

The authors declare that there is no conflict of interest.

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