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Hypolipidemic Effects of Seed Extract of Celery (*Apium graveolens*) in Rats

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ABSTRACT

The hypolipidemic effects of ethanol extract of *A. graveolens* L. (Apiaceae) were investigated. Forty adult male albino rats weighing about 260 g each, were divided into four groups (n = 10). Experimental animals were gavaged at doses of 213 and 425 mg/kg body wt. for sixty consecutive days. Extract showed a significant decrease ($p<0.05$) of serum total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-c), and significant increase ($p<0.05$) in high-density lipoprotein cholesterol (HDL-c) in the treated groups. The oral administration of ethanol extract of *A. graveolens* revealed good hypolipideamic effects in adult male albino rats. The results have given a considerable agreement to the traditional use of *A. graveolens* in the treatment of hyperlipidemia; it could possibly lead to appropriate changes in blood lipid profiles.

KEYWORDS: *Apium graveolens*, hyperlipidemia, HDL cholesterol, LDL cholesterol, triglycerides

INTRODUCTION

Hyperlipidemia contributes significantly in the manifestation and development of atherosclerosis and coronary heart diseases (CHD). Cardiovascular diseases, including atherosclerosis are the most common cause of mortality and morbidity worldwide (1). (Yokozawa et al., 2003). Although several factors, such as diet rich in saturated fats and cholesterol, age, family history, hypertension and life style play a significant role in causing heart failure, the high levels of cholesterol particularly LDL cholesterol are mainly responsible for the onset of CHDs (Farias et al., 1996 and Yokozawa et al., 2003). Lowering lipids and cholesterol levels by a drug or dietary interventions could reduce the risk of CHD. Current interest in natural products has stimulated the search for new cholesterol-lowering agents from these sources. Many herbal medicinal products were reported to have a potential to reduce lipid and cholesterol in body and to enhance the safety profile. Several studies have reported that the hydroalcohol extract obtained from the leaves of *Croton cajucara* (Euphorbiaceous) has a significant reduction in serum total cholesterol (Tc), and low-density lipoprotein cholesterol (LDL-c) levels without significant change in serum high-density lipoprotein cholesterol (HDL-c) and triglycerides (TG) (Devi and Sharma, 2004; Patil et al., 2004; Shukla et al., 2004; Farias et al., 1996). The data also showed a significant elevation in the HDL-c/

Tc ratio in plant extract treated rats compared with the control group. Choudhary et al. (2005) were found that the ethanol extract of *Iris germanica L.* (Iridaceous) significantly lowered the lipid components especially, the cholesterol and triglycerides. It was shown that *A. graveolens* extracts have different beneficial biological activities as it reported by Jiao et al. (2003) concerning its antibiotic activity. The isolated compounds from the seeds exhibited antioxidant and inhibitory effects of cyclooxygenase and topoisomerase enzymes (type I and II) (Momin and Nair, 2002). The methanol extract of celery showed a significant hepatoprotictive activity compared to the paracetamol and thioacetamidein treated rats (Singh and Handa, 1995; Bahar et al., 2002). Celery was also found to have anticarcinogenic and antiproliferation activities (Sultan et al. 2005). *A. graveolens* was reported to exhibit anti-inflammatory activity in experimental animals (AL-Hindawi et al., 1989; Atta and Alkofahi 1998). Celery seeds have gastro protective effect probably mediated through non-prostaglandin E2 production (Whitehouse et al., 2001). Extracts of root and leaves of *A. graveolens* show a potential activity as scavenger of free OH and DPPH radicals as well as inhibiting of the liposomal peroxidation. Therefore, they can act as antioxidants (Popovic et al., 2006). The part of celery extract responsible for the hypocholesterolaemic action is the sugar or amino acid side chains, which mainly lowered the total cholesterol level by increasing the bile acid excretion (Tsi et al., 1995: Tsi and Tsi 2000). Ko et al., (1991) have reported that the apigenin isolated from A. graveolens relaxes rat thoracic aorta mainly by suppressing the Ca^{2+} influx through both voltage- and receptor-operated calcium channels. A significant hepatoprotective activity of the methanol extract of the celery seeds was reported by and (1995). Choochote et al. (2004) who used the hexane fraction of *A. graveolens* seeds reported that it has a strong repellent activity against a wide range of mosquito species belonging to various genera. Therefore, it has been concluded that it can act as an effective personal protection measure against mosquito bites and the diseases caused by mosquito-borne pathogens (Tuetun et al., 2004). The antihyperlipidemic properties of aqueous celery extract was studied in rats and at the end of the experiment, a significant reduction in the serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), and triglyceride (TG) concentrations in the celery-treated rats were observed. However, the concentration of hepatic TG was significantly higher in the celery-treated group than in the control group (Tsi and Tan, 1995, 2000). A previous study was reported that the lab animals that were given a daily dose of a compound extracted from celery seed experienced a 12% reduction in their blood pressure over a four-week period, also it may reduce artery-clogging cholesterol (Blumenthal, 1998). This study was dedicated to monitor changes in the lipid profile of male albino rats under the hypolipidemic effects of celery seed extract.

MATERIAL AND METHODS

Plant processing

Brown carmocarp seeds of *A. graveolens* were purchased from the local market (Amman). The seeds were planted in the green house of the Department of Biological Sciences, Faculty of Science, University of Jordan. The plant was taxonomically identified by direct comparison with authenticate sample and with the help of Prof. Dawoud Al-Eisawi, Department of Biological Sciences, University of Jordan. A voucher specimen (Number APO-05) was deposited at Department of Pharmaceutical Sciences, Faculty of Pharmacy, University of Jordan. *A. graveolens* seeds (3 kg) were finely powdered and infused using hot water overnight. Plant materials were then extracted by Soxhelet apparatus using 96% ethanol for 2 h. The solvent was then distilled off under reduced pressure below 50°C using Rotavapor. The dark brown residual extract which equal to 188 g was kept in refrigerator at 4°C until use. The yield of the ethanol extract was 6.26%.

TLC screening

Plant extracts were applied to pre-coated TLC silica gel plates (silica gel 60 F_{254}, AluGram, Germany) developed in appropriate solvent systems and visualized using different reagents according to the type of secondary metabolites under investigation. Chromatograms were examined before and after spraying under UV and daylight to detect the presence of flavonoids, coumarins, alkaloids and terpenes (Table 1).

Preparation of doses

Doses were prepared by dissolving 4.54 and 9.07 g of the ethanol extract in total volume of 84 ml solution (83 ml normal saline and 1 ml Tween 20) to give 213 and 425 mg/

Table1. Phytochemical screening of the water and ethanol extracts of *A. graveolens* seeds.

Compound	Water extract	Ethanol extract
Flavonoids	+	+++
Coumarins	+	++
Alkaloids	−	−
Terpenoids	+	+++

(−): Not detected , (+): Weak present (++): Moderately present, (+++): Strong Present.

kg, respectively. One ml of either dose was gavaged daily to the rats (average weight of 260 g) for 60 consecutive days.

Animal Model

This study was conducted in the experimental animal laboratory of the Faculty of Sciences, University of Jordan. All animals were housed, fed and treated in accordance with the in house guidelines for animal protection to minimize pain and discomfort. Adult male albino rats (Sprague-Dawely strain) weighing about 260 g each were used throughout the study. The animals were left for a week to adapt to the room conditions (temperature, humidity, light and dark period, aeration, and caging). Food and water were provided *ad libitum*. Animals were described as fasted were deprived of food for at least 12 h but were allowed free access to drinking water.

Treatment

Male rats were divided into four groups (n = 10), the body weights for all treated groups were recorded. The first group was considered as a negative control and gavaged with one ml of distilled water, while the second one which is the vehicle group was gavaged with vehicle solution (Tween 20 and normal saline). As for the last two groups, rats were gavaged daily for sixty consecutive days with 1ml of the extract at doses of 213 or 425 mg/kg body wt. No sign of toxicity was noticed on the behavior and general health of the animals when exposed to extract.

Upon gavaging the animals in control and vehicle groups with one ml of the solutions the number of survived animals were recorded after 24 h of treatment. Animals were gavaged with one ml of the prepared doses; 30, 40, 50, 60, 70, 80, 85, 90, 95, 100 mg/20 g. After 24 h of injection the dead and survived animals were recorded (Table 2). The weights of the animals were recorded in all groups before and after the experiment (Table 3).

Table 3. Effect of *A. graveolens* seed extract on body and organs weights in control, vehicle, and treated groups

Groups	Initial weight (g)	Final weight (g)
Control	257 ± 3.8	345.7± 21.8
Vehicle	254 ± 3.7	308.3± 44.7
Dose(1) 213mg/kg	255 ± 3.0	288.3± 44.1*
Dose(2) 425mg/kg	255 ± 3.9	295.0± 46.6*

*Mean ± SD are significant at the 0.05 level.

Blood collecting

After 12-14 h of fasting blood samples were drawn from rats in plain tubes and allowed to clot, the samples were centrifuged to obtain serum using a bench top centrifuge (Cenformix).

Determination of serum glucose and lipid profile

Serum glucose and lipid profile, including: total cholesterol (TC); triglycerides (TG); high-density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c) was determined by using commercial analytical kits from Sigma (St. Louis, Mo, USA).

Statistical analysis

Results are expressed as mean ± SD. The data were analyzed using One way ANOVA followed by multiple comparison test of Dunet. Results are considered significant when P-value is <0.05

RESULTS AND DISCUSSION

TLC screening of the chemical constituents of water and ethanol extracts of *A. graveolens* revealed the presence of flavonoids, coumarins, and terpenoids as major components. These compounds are mainly concentrated in the ethanol extract (Table 1). Depending on these observations and on preliminary investigation, the ethanol extract was chosen to accomplish the animal experiment. Herbal preparation has been used in many parts of the world since ancient times. In recent years, their popular alternative to modern medicine has increased considerably

Table 2. Result of the LD50 experiment

Dose(mg/20g)	30	40	50	60	70	80	85	90	95	100
Total number of the group	7	7	7	7	7	7	7	7	7	7
Number of animals died	0	1	2	1	3	1	1	6	6	7
Number of animals survived	7	6	5	6	4	6	6	1	1	0
Sg	42	35	29	24	18	14	8	2	1	0
Ds	0	1	3	4	7	8	9	15	21	28
Sg + Ds	42	36	32	28	25	22	17	17	22	28
Mortality = Ds/(Sg+Ds)×100%	0	3	9	14	28	36	53	88	95	100

Sg: Number of mice survived at this dose and higher doses
Ds: Number of mice died at this dose and lower doses

even in developing countries (Maurya et al., 2004). In the present study two doses of the extract were chosen to investigate the hypolipidemic effects of seed ethanol extracts of celery in male albino rats. Based on the lethal dose of the seed extracts (85 mg/20 g), two doses were chosen (425 and 213 mg/kg) which were administered by oral gavaging needle.

The result showed a significant ($p<0.05$) body weight loss of the treated groups compared to the control and vehicle groups (Table 3). The exact mechanism by which the plant extract induce weight loss is not well known. However, several studies have shown that agents could cause body weight reduction through several proposed mechanisms. Theses include: stimulation of the mobilization, inhibition of lipoproteinslipase activity, increasing energy expenditure, inhibition of absorption of nutrients from the gastrointestinal tract, suppression of the appetite, and reduction of food intake (Dyer, 1994: Angelica, 1998). After the analysis of red blood cells (RBC), white blood cells (WBC), and packed cellular volume (PCV), in both treated and vehicle groups, the results were within normal range in comparison to the control group (Table 4). Blood performs many functions, so any change in the blood parameters will indicate a toxic effect of the extract on the body. No alteration in hematological parameters: Red blood cells (RBC) count, White blood cells (WBC) count, and packed cellular volume (PCV) in the treated groups compared to the control group. Parveen et al. (2003) showed the similar effect by using the bark chloroform extract of *Quassia amara* L. (Simaroubaceae) and the 70% methanol extract of *Sarcostemma acidum* (Roxb.) Voigt (Simaroubaceae) stem (Verma et al. 2002). No remarkable alternations were recorded in liver enzymes Glutamic-oxaloacetic transaminase (GOT) and Glutamyl pyruvic transaminase (GPT) in both treated and vehicle groups when compared to the control (Table 4). This indicates that *A. graveolens* seed extract may not cause any toxic effect on the body. However, Sultan et al., (2005) reported that the isolated flavonoid, apigenin, act as inhibitory agent against tumor formation in the liver cells. Similar result was reported on the effect of aqueous *Carica papaya* L. (Caricaceae) seeds on liver function enzymes. No changes in the concentrations of these enzymes were observed (Lohiya et al., 2000). In this study, it has also been observed that there is a significant decrease in the concentration of total cholesterol, triglycerides, LDL cholesterol and a significant increase in HDL cholesterol in the treated groups (Table 5). Similar results were observed in the effect of ethanol extract of *Iris germanica* L. rhizomes (Iridaceous), they indicated that ethanol extract of *Iris germanica* has remarkably lowered the lipid components, particularly, the cholesterol and triglycerides (Choudhury et al., 2005). Other researchers showed also that celery seed extract helped in the support of healthy blood pressure and cholesterol levels because of its beneficial effect on prostaglandin levels. Le and Elliott, (1991) at the University of Chicago Medical Center identified it as the factor in celery responsible for the blood pressure lowering effect of celery. The results suggest that the lipid lowering action of this natural product maybe mediated through inhibition of hepatic cholesterol biosynthesis, increased faucal bile acids excretion, and enhanced plasma lecithin: cholesterol acyltransferase activity, and reduction of lipid absorption in the intestine.

Table 4. Hematological and liver function enzymes data (Mean ± SD)

Groups	RBC (10^6Cell/ mm^3blood)	WBC Cell/ mm^3 blood)	PCV (%)	GOT (U/L)	GPT (U/L)
Control	8.9 ± 0.5	8441 ± 1042.3	58 ± 6.9	286 ± 71.2	67 ± 18.6
Vehicle	8.2 ± 0.2	8070 ± 864.0	64 ± 4.9	270 ± 160.0	71 ± 24.5
Dose(1) 213mg/kg	8.3 ± 0.3	8260 ± 1154.7	63 ± 3.7	224 ± 70.3	53 ± 13.5
Dose(2) 425mg/kg	8.1 ± 0.5	8235 ± 962.1	60 ± 9.3	264 ± 134.9	63 ± 21.9

*Significantly different between control group and treated groups $p<0.05$

Table 5. Effect of treatment with ethanol extract of *A. graveolens* on serum glucose and lipid profile concentration in control and treated rats.

Parameter	Control	Vehicle	Dose (1) 213 mg/kg	Dose (2) 425 mg/kg
Cholesterol (mg/dl)	106.2 ± 8.	102.9 ±11.2	94.8 ± 7.92*	89.5 ± 9.1
Triglycerides (mg/dl)	78.7 ± 10.5	75.6 ± 11.6	62.3 ± 9.23*	58.9 ± 5.64*
HDL-C (mg/dl)	38.4 ± 3.8	36.1 ± 1.8	44.5 ± 3.10*	46.2 ± 3.27*
LDL-C(mg/dl)	28.5 ± 3.38	29.7 ± 2.51	4.4 ± 6.2*	21.8 ± 4.59*
Glucose (mg/dl)	96.6 ± 7.3	93.2 ± 5.1	86.8 ± 4.7	84.3 ± 5.2

*Significantly difference between control and treated groups ($p<0.05$)

CONCLUSION

Apium graveolens L. has shown good antihyperlipidemic effect and could be of value in reducing serum total cholesterol, triglycerides, LDL-c and increasing HDL-c.

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