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Original article

Determination of the regulatory properties of *Yucca schidigera* extracts on the biochemical parameters and plasma hormone levels associated with obesity

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ABSTRACT

Yucca schidigera Ortgies, Asparagaceae, is a herbaceous plant. Due to the high saponin content the powdered branches and leaves are used as natural food additive for human and animal. The aim of this study was to investigate the effects of *Y. schidigera* extracts on plasma leptin, ghrelin, adiponectin, insulin, thyroid hormones and some biochemical parameters in mice fed a high-fat diet. Male Swiss Albino mice were divided into seven equal groups. Group I (negative control group) was given standard diet; Group II was given high-fat diet; Group III was given high-fat diet with carboxymethylcellulose; Groups IV–VII were given hexane, petroleum ether, ethyl acetate, and methanol extracts of *Y. schidigera* and high-fat diet via gastric gavage for 60 days. High-fat diet significantly increased plasma leptin, insulin, free T_3 hormone, glucose, cholesterol, low-density lipoprotein, triacylglyceride, aspartate aminotransferase and alanine aminotransferase levels, and significantly decreased plasma ghrelin, adiponectin and free T_4 hormone levels. On the other hand, hormone levels, lipid profile and biochemical parameters were improved by the administration of the PE extract. *Y. schidigera* extracts could be used as preventive medicine in nutritional disorders via regulating energy metabolism and hormonal functions.

Introduction

Yucca schidigera Ortgies is a herbaceous plant from the family Asparagaceae, native to the deserts of the south-western United States and northern Mexico. Due to the antiprotozoal and antifungal properties and hormone-stimulating effects it has been used safely to enhance performance as feed material for livestock as well as food material for humans (Narutoshi, 1992). Moreover, in recent researches, *Y. schidigera* has shown to possess antioxidant, anti-hypercholesterolemic, anticarcinogenic, antiarthritic, anti-inflammatory, antiprotozoal, antifungal and antihypertensive properties. The plant was shown to have secondary metabolites such as eugenol, caffeic acid, rosmarinic acid and α-tocopherol. Moreover, the dried and powdered plant material also contains approximately 10% steroidal saponins and is used commercially as a saponin source (Francis et al., 2002; Piacente et al., 2004; Enginar et al., 2006; Kucukkurt and Dündar, 2013).

Saponins are a class of secondary metabolites found in several plant species. More specifically, they produce soap-like foaming when shaken in aqueous solutions, and, in terms of structure, one or more hydrophilic glycoside moieties combined with a lipophilic triterpene or steroidal aglycone. These compounds are used in phytotherapy and in the cosmetic industry for their cytotoxic, hemolytic, molluscicidal, anti-inflammatory, antifungal, antiyeast, antibacterial and antiviral activities (Leung et al., 1997; Sen et al., 1998; Bachran et al., 2006) as well as in the pharmaceutical industry for the semi-synthesis of steroidal drugs (Chwalek et al., 2006). Moreover, saponins stimulate luteinizing hormone release leading to abortifacient properties (Francis et al., 2002), have immunomodulatory potential (Sun et al., 2009), cytostatic and cytotoxic effects (Bachran et al., 2008) and adjuvant properties for vaccines (Sjolander et al., 1998). Due to their physiological properties, saponins are now expected to serve as functional components in food. They have been reported to decrease plasma cholesterol

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in rats when added to their diets (Oakenfull, 1981; Sidhu and Oakenfull, 1986).

Fatty diet, as well as imbalance between the food intake and energy expenditure are the factors affecting the prevalence of obesity (Altunkaynak, 2005; Milagro et al., 2006). Obesity and overweight pose a major risk for serious diet-related chronic diseases, including type-II diabetes, cardiovascular diseases, hypertension, stroke and certain forms of cancer. Leptin, insulin and T_3 are among the most important hormones to provide this balance (Otukonyong et al., 2005). Leptin, an adipose tissue hormone, regulates body fat mass and body weight by decreasing the appetite and increasing energy expenditure (Zabrocka et al., 2006).

The present study was planned to determine the effects of the extracts obtained from *Y. schidigera*, which was reported to be rich in saponins in the previous studies, on leptin, ghrelin, insulin and thyroid hormones and some biochemical parameters in mice fed a high-fat diet.

Materials and methods

Plant material

Yucca schidigera Ortgies, Asparagaceae, standard powder (Sarsaponin 30® contains more than 8% steroidal saponin) was purchased from Desert King International (San Diego, CA, USA).

Preparation of the extracts

Y. schidigera powder (500 g) was successively extracted with 5 l of hexane (HE), petroleum ether (PE), ethyl acetate (EA) and methanol (ME) by percolation method at room temperature. After completion of extraction the extracts were filtered and the solvent was removed by distillation under reduced pressure and low temperature (40–50 °C) on a rotary evaporator to give crude extracts. Extracts were weighed and yield percentages were calculated as 17.93% for HE, 26.42% for PE, 11.02% for EA and 9.27% for ME.

Animals

Male Swiss Albino mice (25–35 g) were purchased from the animal breeding laboratories of Afyon Kocatepe University Experimental Animal Research and Application Center (Afyon, Turkey). The animals were allowed to acclimatize to the animal facility for at least 7 day before experiment started. The room conditions were maintained in a 12 h light/12 h dark cycle at room temperature (25 ± 3 °C), with rodent standard diet and water provided ad libitum. A minimum of ten animals was used in each group. The study was permitted by the Institutional Animal Ethics Committee (Ankara University Ethical Council Study Number: 2009/34) and was performed according to the international rules considering the animal experiments and biodiversity right.

Experimental protocol

Two different control groups were employed in the study. The negative control group was maintained on standard pellet diet and water ad libitum without administering any plant extract (negative control group). The high-fat diet (HFD) group received special diet containing 40% beef tallow for eight weeks (HFD group-positive control). The vehicle control group received 0.5% CMC suspension in distilled water and was maintained on HFD (CMC group). On the other hand, the experimental group animals received hexane (HE), petroleum ether (PE), ethyl acetate (EA), and methanol (ME) extracts obtained from *Y. schidigera* along with HFD. Extracts were administered orally after suspending in distilled water and 0.5% sodium carboxymethyl cellulose (CMC) by using a gastric gavage at 100 mg/kg doses daily for eight weeks. This dose was determined according to a previous preliminary study (Avci et al., 2006). Blood samples were taken from the heart into tubes with heparin and plasma was obtained at the end of the experimental period, then centrifugation performed at 1500 × *g* (+4 °C) for 10 min and kept at −30 °C in advance of assays.

Biochemical analysis

Plasma leptin (Biovendor, Czech Republic, Cat No. RD291001200R), insulin (Millipore, USA, Cat No. EZRMI-13K), ghrelin (Millipore, USA, Cat No. EZRGRT-91K), total adinopectin (Biovendor, Czech Republic, Cat No. RD293023100R), total tri-iodothyronine (T_3) (DRG International Inc., USA, Cat No. EIA-4569), total tetra-iodothyronine (T_4) (DRG International Inc., USA, Cat No. EIA 4568), free tri-iodothyronine (FT3) (DRG International Inc., USA, Cat No. EIA-2385) and free tetra-iodothyronine (FT4) (DRG. International Inc., USA, Cat No. EIA 2386) were measured using an enzyme-linked immunosorbent assay (ELISA).

Liver damage was assessed by the estimation of serum levels of alanine aminotransferase (ALT), and aspartate aminotransferase (AST) by using commercial kits Teco Diagnostics assay kit (Teco Diagnostics, CA, USA). Serum levels of total protein (Tp), urea, total cholesterol (Tc), glucose, low density lipoprotein-cholesterol (LDL-c), high density lipoprotein-cholesterol (HDL-c) and triacylglyceride (Tg) were determined using COBAS test kits (Roche Diagnostics Systems, Istanbul, Turkey) according to the manufacturers' instructions in Laboratory of Biochemistry, Faculty of Veterinary Medicine, University of Afyon Kocatepe (Turkey).

Statistical analysis of data

The data obtained from the animal experiments was expressed as mean and standard error (±SEM). The statistical differences among the experimental groups were evaluated by one-way ANOVA and Duncan post hoc tests using the SPSS computer software program. A difference of $p < 0.05$ in the mean values was considered significant.

Results

Body weights of the mice are shown in Table 1. Supplementation of HFD to the animals during eight weeks significantly increased the body weight compared to the control group ($p < 0.05$). On the other hand, during the experimental period PE extract prevented the weight gain of mice compared to the other groups.

Plasma glucose, TC, LDL, HDL, TG, AST, and ALP were found to be high in HFD and CMC + HFD groups compared to the control group ($p < 0.05$) as shown in Table 2. On the other hand, administration of 100 mg/kg *Y. schidigera* extracts, especially HE and PE, decreased the levels of these parameters ($p < 0.05$). These results suggest that *Y. schidigera* extracts have capacity to alleviate the biochemical status caused by HFD.

Supplementation of HFD increased leptin, insulin, and FT3 whereas decreased ghrelin, adiponectin, and FT4 ($p < 0.05$). In addition, TT4 and TT3 levels were not changed in all groups (Table 3). On the other hand, administration of 100 mg/kg *Y. schidigera* extracts especially PE resulted in reversal of HFD-induced hormone levels ($p < 0.05$). These results suggest that *Y. schidigera* extracts affected hormone status.

Discussion

Although in some studies it was shown that HFD does not affect weight gain (Gao et al., 2002), in our study it was observed that

Table 1
The effects of *Yucca shidigera* extracts on body weight in mice (*n*: 15; mean ± SEM).

Groups	0 day	15 day	30 day	45 day	60 day	*p* value
Control	25.43 ± 0.75	25.57 ± 0.67	25.17 ± 0.69	25.61 ± 0.87	26.00 ± 0.99	0.966
HFD	26.44 ± 0.79^{c}	29.44 ± 1.02^{b}	32.27 ± 1.20^{b}	35.40 ± 1.06^{a}	36.90 ± 1.18^{a}	0.000
HFD + CMC	26.19 ± 0.82^{c}	29.61 ± 1.21^{b}	31.86 ± 1.28^{b}	36.16 ± 0.93^{a}	36.63 ± 1.21^{a}	0.000
HE extract	25.86 ± 1.06^{b}	30.85 ± 0.98^{a}	29.47 ± 1.44^{a}	30.01 ± 1.10^{a}	30.08 ± 0.98^{a}	0.038
PE extract	26.93 ± 1.36	30.31 ± 1.77	30.20 ± 0.89	30.81 ± 0.88	30.68 ± 1.04	0.083
EA extract	27.87 ± 1.49^{b}	31.60 ± 1.42^{a}	31.76 ± 1.26^{a}	33.86 ± 1.08^{a}	34.19 ± 1.08^{a}	0.012
ME extract	26.17 ± 0.87^{b}	33.31 ± 0.74^{a}	33.27 ± 0.77^{a}	33.90 ± 0.72^{a}	34.64 ± 0.72^{a}	0.000

^{a,b,c} Values with different letters within a column are significantly different by Duncan's multiple range test.
HE, hexane; PE, petroleum ether; EA, ethyl acetate; ME, methanol.

Table 2
The effects of *Yucca schidigera* extracts on blood biochemical parameters in mice (*n*: 15; mean ± SEM).

Groups	Glucose (mg/dl)	Tc (mg/dl)	LDL-c (mg/dl)	HDL-c (mg/dl)	Tg (mg/dl)	Tp (g/dl)	AST (U/L)	ALT (U/L)
Control	103.6 ± 2.50^{cd}	88.71 ± 2.69^{c}	22.30 ± 2.59^{c}	85.66 ± 2.45^{c}	64.37 ± 3.16^{bc}	4.30 ± 0.08	39.34 ± 4.09^{b}	164.1 ± 11.3^{b}
HFD	163.7 ± 9.28^{a*}	189.1 ± 8.45^{a*}	66.7 ± 6.47^{a*}	116.8 ± 2.71^{b*}	99.85 ± 4.25^{a*}	4.34 ± 0.15	76.19 ± 4.48^{a*}	235.5 ± 23.8^{a*}
HFD + CMC	179.5 ± 7.47^{a}	197.6 ± 14.31^{a}	70.6 ± 3.13^{a}	118.2 ± 4.37^{b}	102.9 ± 5.14^{a}	4.37 ± 0.12	71.68 ± 5.02^{a}	241.7 ± 20.1^{a}
HE extract	91.03 ± 3.01^{d}	137.7 ± 8.65^{b}	49.32 ± 1.99^{b}	139.1 ± 6.09^{a}	76.00 ± 4.55^{b}	4.83 ± 0.12	36.28 ± 2.93^{b}	173.1 ± 13.1^{b}
PE extract	118.2 ± 7.35^{c}	129.3 ± 5.29^{b}	42.97 ± 1.48^{b}	111.3 ± 3.96^{b}	66.71 ± 3.74^{bc}	4.77 ± 0.12	46.26 ± 2.42^{b}	179.3 ± 12.1^{b}
EA extract	124.1 ± 7.17^{c}	128.2 ± 3.06^{b}	62.64 ± 4.94^{a}	108.6 ± 3.61^{b}	57.01 ± 5.01^{c}	4.50 ± 0.18	36.80 ± 2.97^{b}	173.9 ± 14.6^{b}
ME extract	148.4 ± 13.2^{b}	148.5 ± 6.81^{b}	65.0 ± 3.97^{a}	124.4 ± 9.03^{b}	66.43 ± 6.82^{bc}	4.31 ± 0.23	44.09 ± 2.99^{b}	180.1 ± 10.8^{b}
p value	0.000	0.000	0.000	0.000	0.000	0.067	0.000	0.003

* HFD group is statistically different compared to the control group ($p < 0.05$)
^{a,b,c} Values with different letters within a column are significantly different by Duncan's multiple range test ($p < 0.05$).
HE, hexane; PE, petroleum ether; EA, ethyl acetate; ME, methanol.

mice given fat exhibited weight gain as in the long term studies carried out with HFD (Cha et al., 2000). Compared to the control group, the increase in 15 days live weight was found to be statistically significant in all groups but the PE and HE groups. The other measurements were also supported these data.

Although body fat index and body mass index are the major determinants of leptin levels, insulin, glucocorticoids and prolactin stimulate leptin synthesis while NPL, thyroid hormones, GH, somatostatin, free fatty acids and long exposure to cold inhibit it (Kucukkurt, 2015). In a previous study by İşbilen et al. (2007) HFD fed rats during five weeks, the plasma, aort and liver leptin levels increased. Similarly, in our study, plasma leptin levels increased in the high-fat diet and CMC groups. In *Y. schidigera* extract groups, however, leptin levels decreased significantly although mice were fed a high-fat diet. The decrease of leptin levels in the extract groups and increase in high-fat diet groups were parallel with the changes in the live-weight as shown in Table 1. Indeed, Kim et al. (2005) fed the rats with high-fat diet for eight weeks and then refined the steroidal saponins in Red Korean Ginseng, which is considered as a steroidal saponin source like *Y. schidigera*, and administered it intraperitoneally for three weeks at a dose of 200 mg/kg/day. At the end of the study, it was noted that plasma leptin levels decreased significantly in the animals that were given saponin, and the researchers suggested that this could be due to the fact that saponin resulted in decrease in live-weight and body fat mass. In another study by the same researchers, protopanaxadiol and protopanaxatriol-type saponins from Red Ginseng were administered to the rats fed a HFD at 50 mg/kg/day dose. It was reported that the decrease in plasma leptin levels could be attributed to thermogenesis properties of the saponins (Kim et al., 2009). The mentioned researches on the activity of the saponins on the leptin levels, supported our results which reveal a decrease in body fat mass in mice with the administration of *Y. schidigera* extracts.

Consistent with these findings, in our study, both ghrelin and adinopectin levels decreased significantly in the mice fed a HFD compared to the control group. Ghrelin levels increased in the PE and HE groups while they did not change in the other extract groups. This increase in the PE and HE groups is consistent with the decrease in leptin levels and live-weight. In the other extract groups, no change was seen in ghrelin hormone levels compared to the HFD group and in these groups live-weight decrease was not similar to that in the PE and HE groups. In our study, insulin hormone increased statistically, particularly in the HFD and CMC groups. Increase in insulin reflects that blood glucose was stored as glycogen in the liver and as fatty acids in the adipose tissue (Bayşu Sözbilir and Bayşu, 2008). Increase in adipose tissue also

Table 3
The effects of *Yucca schidigera* extracts on some hormones in mice (*n*: 15; mean ± SEM).

Groups	Leptin (ng/ml)	Ghrelin (mg/dl)	Adiponectin (mg/dl)	Insulin (ng/ml)	TT4 (μg/dl)	ST4 (ng/ml)	TT3 (μg/dl)	ST3 (pg/ml)
Control	28.14 ± 1.75^{b}	1.21 ± 0.05^{a}	1.41 ± 0.13^{a}	0.44 ± 0.05^{c}	34.45 ± 3.45	0.36 ± 0.04^{a}	18.33 ± 0.15	1.91 ± 0.05^{b}
HFD	57.41 ± 4.13^{a*}	0.79 ± 0.06^{b*}	0.79 ± 0.09^{b*}	2.07 ± 0.24^{a*}	41.39 ± 1.22	0.14 ± 0.02^{b*}	18.58 ± 0.14	3.52 ± 0.33^{a*}
HFD + CMC	54.24 ± 4.81^{a}	0.73 ± 0.04^{b}	0.81 ± 0.11^{b}	2.21 ± 0.15^{a}	42.44 ± 2.47	0.15 ± 0.02^{b}	18.90 ± 0.26	3.03 ± 0.31^{a}
HE extract	36.55 ± 2.04^{b}	0.81 ± 0.04^{b}	1.49 ± 0.12^{a}	0.56 ± 0.11^{bc}	36.89 ± 1.53	0.42 ± 0.04^{a}	18.41 ± 0.04	3.25 ± 0.17^{a}
PE extract	36.05 ± 3.13^{b}	1.38 ± 0.07^{a}	1.52 ± 0.08^{a}	0.80 ± 0.04^{bc}	43.54 ± 2.57	0.49 ± 0.05^{a}	18.44 ± 0.03	3.26 ± 0.09^{a}
EA extract	37.81 ± 5.72^{b}	0.77 ± 0.07^{b}	1.21 ± 0.11^{a}	0.84 ± 0.04^{b}	43.70 ± 3.37	0.50 ± 0.04^{a}	18.47 ± 0.09	3.16 ± 0.18^{a}
ME extract	35.39 ± 2.27^{b}	0.75 ± 0.09^{b}	1.46 ± 0.10^{a}	0.79 ± 0.12^{bc}	40.02 ± 2.88	0.44 ± 0.07^{a}	18.45 ± 0.05	3.19 ± 0.07^{a}
p value	0.000	0.000	0.000	0.000	0.126	0.000	0.098	0.000

* HFD group is statistically different compared to the control group ($p < 0.05$).
^{a,b,c} Values with different letters within a column are significantly different by Duncan's multiple range test ($p < 0.05$).
HE, hexane; PE, petroleum ether; EA, ethyl acetate; ME, methanol.

increases leptin hormone levels in the blood (Patel et al., 1998). Srinivasan et al. (2005) reported that body weight increases in rats fed a HFD, which leads to increase in plasma glucose, triacylglyceride, total cholesterol and insulin levels compared to the control group. Besides, Winzell and Ahren (2004) studied the effect of HFD and reported that insulin levels increase in mice parallel to feeding on a HFD. In the present study, the same situation was seen in the HFD group, however, insulin levels decreased in the *Y. schidigera* extract administered-groups suggesting that active ingredients found in extracts may probably play a role in this action. A review by Margetic et al. revealed that many studies conducted in humans and rats suggest that hyperinsulinemic conditions increase plasma leptin levels. Patel et al. (1998) reported that plasma leptin levels decrease in diabetic rats, but administration of insulin acts by increasing plasma leptin levels. Our findings are found to be in accord with those previous data.

Considering thyroid hormone measurements, although in our study there was not any difference between the total T_4 and T_3 and free T_3 levels increased, free T_4 hormone decreased in the *Y. schidigera* extract groups compared to the HFD and CMC groups and we did not note any change compared to control group. Our previous study shows that escin which contains saponin effects serum T_3 and T_4 levels in HFD fed mice (Avci et al., 2010). Although we did not spot any study in literature that focus especially on saponins and thyroid hormones, there are data suggesting that short- and long-term use of natural and synthetic flavanoids cause decrease in plasma T_3 and T_4 levels (Van der Heidi et al., 2003). Fain et al. (1997) found that administration of T_3 to hypothyroid rats decreased leptin mRNA levels by 40% at the 8th hour; therefore, they suggested high thyroid hormone levels can diminish leptin levels. Zabrocka et al. (2006) showed that serum leptin levels and white adipose tissue mRNA levels that are considered as indicators of leptin synthesis decrease in rats, to which they had given various amounts of T_3. In some studies, however, no correlation was reported between thyroid hormones and leptin (Friedman and Halaas, 1998).

Studies show that HFD increases ALT and AST levels in the blood (Friedman et al., 1996). In this study, it was also observed that plasma AST and ALT levels increased and this increase was less in the *Y. schidigera* plant extract groups. The plant *Y. schidigera* contains mainly steroidal saponins as well as vegetal chemicals such as phenolic substances, fiber, resveratrol and stilbens in its dry matter and these saponins are widely used in industry and stockbreeding (Kucukkurt and Dündar, 2013). It was showed in several studies that plants containing saponin act by reducing the absorption of nutritions in the digestive tract and can alter metabolism by this route. *Y. schidigera* lowers lipid metabolism and blood glucose levels. It is thought that these effects of saponins are revealed when taken in small amounts and they particularly alter normal absorption of lipids and glucose in the digestive tract (Kucukkurt and Dündar, 2013). *Y. schidigera* acts on lipid metabolism and lowers cholesterol, LDL and triacylglyceride levels (Kim et al., 2003; Kucukkurt et al., 2011). When the extract groups were taken into account, the lowest value that decreased glucose levels of all the groups was the HE-administered group. While a decrease in cholesterol and triacylglyceride levels was noted in all the extract groups, LDL levels decreased only in the HE and PE groups. Findings in this study indicate the effect of *Y. schidigera* on lipid metabolism and similar results were also obtained in the other studies (Ince et al., 2013; Kucukkurt and Dündar, 2013). Here, *Y. schidigera* generated a regulatory effect on the lipid profile and lipid metabolism by regulating hepatic functions. As a conclusion, extracts obtained from *Y. schidigera* can be used for the prevention of the diseases caused by HDF and regulation of the energy metabolism and hormonal functions. Petroleum ether and hexane extracts exert the most significant effect, yet, further studies should be conducted to reveal the active secondary metabolites.

Authors' contributions

IK, FK and NBS contributed to biochemical analyses. EKA and IS contributed in the selection of the plant material, preparation of the plant extracts and writing the manuscript. SI and AE contributed in the application of the test materials to the animals. All the authors have read the final manuscript and approved the submission.

Conflicts of interest

The authors declare no conflicts of interest.

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