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Original Article

Effects of the Aqueous Extract from *Abelmoschus esculentus* L Peel on Hyperglycemia and Hyperlipidemia Induced by Dexamethasone in Rats

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Abstract

Background: Hyperglycemia and hyperlipidemias are common clinical problem among users of glucocorticoids (GCs). The aim of the present study was to explore the effect of oral administration of the aqueous extract of *Abelmoschus esculentus* peel (AEPE) on hyperglycemia and hyperlipidemia induced in rats by dexamethasone (DEXA). **Methods:** Twenty-four rats were randomly divided into four equal groups. Each group was treated for 10 days either with 2% carboxymethylcellulose orally (normal control); 10 mg/kg DEXA subcutaneously (hyperglycemic group); 100 mg/kg AEPE orally plus 10 mg/kg DEXA subcutaneously (treatment group 1); or 200 mg/kg AEPE orally plus 10 mg/kg DEXA subcutaneously (treatment group 2). Animals were killed after 10 days of treatments by decapitation, their blood collected for the analysis of blood sugar and lipid profile. **Results:** Treatment with DEXA induced a significant increase in blood glucose and all lipids and a significant reduction in body weights. After 10 days of treatment, 100 mg/kg of AEPE was able to significantly reduce the effect of DEXA on triglycerides and low-density lipoprotein (LDL) only. 200 mg/kg of AEPE was able to significantly reduce the effect of DEXA on blood glucose levels, cholesterol, triglycerides, and LDL. Both doses of AEPE were able to increase high-density lipoprotein. **Conclusion:** This study suggests that the AEPE could be beneficial in protecting against GC-induced hyperglycemia and hyperlipidemia.

Keywords: *Abelmoschus esculentus,* dexamethasone, hyperglycemia, hyperlipidemia, okra

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.[1] Hyperlipidemia is a common manifestation of type 1 and type 2 diabetes and imposes a high risk for cardiovascular diseases. In Libya, many patients with diabetes, in addition to medical therapy, are using several natural products as remedies.[2] *Abelmoschus esculentus* (AE) (L.) Moench., synonym of okra, also known as lady's fingers or gumbo is a flowering plant from the mallow family.[3] It is valued for its edible green seed pods. It is an important vegetable and widely distributed from Africa to Asia, Southern Europe, and America.[4] The fibers in okra were suggested to help in stabilizing blood sugar by regulating the rate of sugar absorption from the intestinal tract normalizing blood sugar and cholesterol levels.[5,6] Previous studies reported that the polysaccharide in okra possesses anticomplementary and hypoglycemic activity in normal mice[7] and can lower cholesterol level in blood by its ability to bind bile acids.[8] Sabitha *et al*.[9] have found that oral administration of the aqueous extract of AE (L.) produced a significant hypoglycemic effect in streptozotocin-induced diabetes mellitus in rats and with a significant reduction in lipid profile compared to diabetic control group. The extract of AE *per se* was also found to possess a hypoglycemic effect in mice with no observable changes in behavior.[10]

Dexamethasone (DEXA) is a very potent and highly selective glucocorticoid (GC) having profound anti-inflammatory and immunosuppressive properties that are critical for

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the treatment of rheumatoid arthritis, cerebral edema, allergic reactions, asthma, and certain types of cancer.[11] Unfortunately, the development of major metabolic side effects remains the key limitation for the long-term use of GCs. Common side effects requiring dosage adjustment or cessation of treatment include diabetes, hypertension, osteoporosis, and muscle wasting.[12] The odds ratio for new-onset diabetes mellitus in GC-receiving patients ranges from 1.5 to 2.5 and the risk increases proportionally with increasing the GC dosage.[13]

Therefore, this study was aimed to investigate the protective effect of AE peel extract in rats against DEXA-induced hyperglycemia and hyperlipidemia.

Materials and Methods

Animals

Male Wistar albino rats weighing between 150 and 250 g were used. The animals were housed in the animal care facility in the Department of Pharmacology and Clinical Pharmacy and maintained at 23°C with a 12:12 h light: Dark cycle. Animals were kept fasting, overnight, 1 day before starting the experiment.

Plant material and preparation of the aqueous extract

AE was collected from the local market, Tripoli, Libya. The pods were thoroughly washed with tap water and then with distilled water. Seeds were removed, and the peel was dried under shade for 2 weeks, made into coarse powder in a grinder and was stored in an airtight container, up to the completion of the study. Fresh solutions were prepared using 2% carboxymethylcellulose (CMC) as vehicle to disperse the powder of AE.

Drugs and chemicals

DEXA sodium phosphate (Dexone®, Dorcas pharmaceutical laboratories, Sousse, Tunisia), glibenclamide tablet (Gliboral, Menarini International., Pisa, Italy), CMC and diethyl ether were obtained from BDH Chemicals Ltd., Poole, England).

Induction of hyperglycemia and hyperlipidemia

Hyperglycemia and hyperlipidemia were done by subcutaneous administration of DEXA (10 mg/kg for 10 days) according to the procedure described by Shalam *et al*.[14]

Experimental design

Animals were fasted overnight before starting the experiments. Rats were weighed and then were divided into four groups of six rats each. Group 1 is the normal control received 2% CMC (5 ml/kg/day for 10 days) orally. Group 2: (DEXA-treated group) received 10 mg/kg DEXA subcutaneously for 10 days. Group 3: (treatment group 1) received 100 mg/kg *A. esculentus* peel extract (AEPE) orally along with 10 mg/kg DEXA subcutaneously for 10 days. Group 4: (treatment group 2) received 200 mg/kg AEPE orally along with 10 mg/kg DEXA subcutaneously for 10 days.

After treatment period, body weight was measured, and animals were sacrificed by decapitation, their trunk blood was collected directly into a centrifuge tube and allowed to clot for 45–60 min at room temperature. Serum was separated by centrifugation at 2500 rpm for 15 min and analyzed for the following biochemical parameters: total cholesterol (TC), triglycerides (TG) not triglycerides (GL), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) by Cobas integra® 400 (Roche, Switzerland) using commercial kits (Roche-Cobas, Switzerland) according to the manufacturer's protocol. Blood glucose levels were measured using Oncall® Plus glucometer with the corresponding Oncall® test strips, (Acon laboratories, Inc., San Diego, CA, USA).

Statistical analysis

The values were expressed as mean ± standard error. Data were analyzed using SPSS version 17.0 (SPSS Inc., USA). The differences between groups were analyzed using unpaired Student's *t*-test. $P < 0.05$ was considered statistically significant.

Results

A significant reduction in body weight was observed in the DEXA-treated group, and AEPE (200 mg/kg) plus DEXA-treated group compared to vehicle control group [Table 1].

Animals treated with DEXA only showed a significant increase in fasting blood glucose levels (132.71%) compared to vehicle control group. Oral administration of 200 mg/kg of AEPE reduced significantly blood glucose levels to 76.24% of DEXA-treated group [23.76% - Table 1].

DEXA produced a significant increase in TC, TG, HDL, and LDL when compared to control vehicle-treated group. A total of 100 mg/kg of AEPE was able significantly to reduce the effect of DEXA on TG and LDL while potentiating its effect on HDL. On the other hand, 200 mg/kg of AEPE was able to antagonize the effect of DEXA on TC, TG, and LDL, while potentiating its effect on HDL [Table 1].

Discussion

DEXA is a potent GC with many therapeutic applications. High exposure to GCs impairs insulin sensitivity, contributing to the generation of metabolic syndrome including insulin resistance, and hypertension.[15] DEXA also increases TG causing an imbalance in lipid metabolism leading to hyperlipidemia[16] and increases glucose levels leading to hyperglycemia.[17] These serious side effects of GCs require special attention and limit their clinical applications.

AE (Okra) is a popular healthy food due to its high fiber, Vitamin C, and folate contents. Okra is also known for being high in antioxidants and is a good source of calcium and potassium.[18] It was also reported that AEPE possesses hypoglycemic effect against streptozotocin and alloxan-induced diabetes in rats.[19,20] In view of the forwarded mentioned facts, we decided to examine the possibility of a

Table 1: Effect of the aqueous extract of *Abelmoschus esculentus* peel on body weight, fasting blood glucose, and lipid profile

	BW (g)	FBG (mg/dl)	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Control vehicle	190.2±10.03	85.0±3.88	58.2±4.07	60.8±2.42	46.3±3.03	18.5±3.03
DEXA only	173.7±2.67*	112.8±6.16*	117.0±12.41**	197.2±8.06**	67.0±2.66***	28.2±2.66**
Percentage compared to control vehicle group	91.3	132.7	201	324.3	144.7	152.4
DEXA + AEPE (100 mg/kg)	179.8±9.71	106.0±2.03**	115.0±22.86**	167.8±5.05***$^{+}$	78.8±3.38***$^{+}$	10.0±3.38**$^{+++}$
Percentage compared to control vehicle group	94.5	124.7	197.6	276	170.2	54
Percentage compared to control DEXA group	103.5	94	98.3	85	117	35.4
DEXA+AEPE (200 mg/kg)	161.8±0.89*$^{+}$	86.0±5.51^{+}	80.3±3.09**$^{++}$	132.8±7.36***$^{+++}$	114.7±3.31***$^{+++}$	8.8±3.31***$^{+++}$
Percentage compared to control vehicle group	85	101	138	218	247.7	47.6
Percentage compared to control DEXA group	93	76	68.6	67.3	171	32.2

Data are expressed as mean±SE (n=6). *P<0.05, **P<0.01, ***P<0.001 significantly different from control vehicle group. ^{+}P<0.05; ^{++}P<0.01, ^{+++}P<0.001 significantly different from the DEXA-treated group. BW: Body weight, FBG: Fasting blood glucose, TC: Total cholesterol, TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SE: Standard error, AEPE: Aqueous extract of *Abelmoschus esculentus* peel, DEXA: Dexamethasone

protective effect of AEPE against the hyperlipidemias and hyperglycemia induced by the DEXA in rats.

Administration of DEXA for 10 days increased levels of glucose, TG, TC, LDL, and HDL accompanied by a decrease in body weights. The high dose of AEPE (200 mg/kg) significantly prevented all the effects of DEXA except those on HDL where it potentiated its effect. One the other hand, the lower dose of AEPE (100 mg/kg) also prevented the effect of DEXA on TG and LDL but potentiated its effect on HDL. Azeez and Kheder[21] have showed that *Gundelia tournefortii* reduced blood glucose in DEXA-induced hyperglycemia in mice and attributed this effect to the presence of flavonoids which stimulate insulin secretion. Lin *et al*.[22] had demonstrated that flowers and fruit of AE were rich in flavonoids. Therefore, it is tempting to speculate that hypoglycemic effect of AEPE in our study may be due to its contents of flavonoids.

Hyperlipidemia is accepted as an independent risk factor for cardiovascular disorders,[23] and therefore, it requires special management. As it has been demonstrated in our study, AEPE especially at the dose of 200 mg/kg significantly reduced blood levels of TC, TG, LDL, and increased the levels of HDL compared to the DEXA-treated group. In support of our findings, Trinh *et al*.[24] have demonstrated that AEPE reduced cholesterol and triglycerides levels in mice made hyperlipidemic by intraperitoneal administration of a single dose of tyloxapol. Moreover, in *invitro* study, it has been shown that okra is able to bind bile acids and hence may reduce their reabsorption from GIT.[8] Thus, the observed effects in our study may be due to ability of AEPE to reduce absorption of cholesterol from the diet or by interfering with cholesterol synthesis in the liver.

Conclusion

This study suggests that the aqueous extract of *A. esculentus* L can be considered as a preventive therapy against GC-induced hyperglycemia and hyperlipidemia in rats as demonstrated by its ability to normalize blood glucose levels and its positive effect on lipid profile.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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ملخص المقال باللغة العربية

آثار مستخلص مائي لقشور نبات الأكورا (البامية) على فرط سكر الدم وفرط شحوم الدم الناجم عن العلاج باديكساميثازون في الجرذان

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الخلفية: يعتبر ارتفاع السكر وفرط دهون الدم مشكلة سريرية شائعة بين مستخدمي الجلوكوكورتيكويد. الهدف من هذه الدراسة هو استكشاف تأثير تناول المستخلص المائي من قشر نبات أبيلموشش إسكولنتوس (البامية) على ارتفاع السكر والدهون في الدم نتيجة الحقن بالـ ديكساميثازون في الفئران.

الطريقة: تم تقسيم أربع وعشرين فئران عشوائيا إلى أربع مجموعات متساوية. تم علاج كل مجموعة لمدة عشرة أيام إما بـ 2٪ كاربوكسي ميثيل سيلولوس عن طريق الفم، أو 10 ملغ / كغ ديكساميثازون تحت الجلد (مجموعة فرط سكر الدم). أو 100 ملغم / كغم المستخلص المائي للبامية فمياً مع 10 ملغ / كغ ديكساميثازون تحت الجلد (مجموعة العلاج 1)؛ أو 200 ملغ / كغم المستخلص المائي للبامية فمياً مع 10 ملغ / كغ ديكساميثازون تحت الجلد (مجموعة العلاج 2). وقتلت الحيوانات بعد 10 أيام من العلاج عن طريق قطع الرأس، وجمع الدم لتحليل السكر والدهون في الدم.

النتائج: نتج عن العلاج بـ ديكساميثازون إلى زيادة ملحوظة في مستوى السكر في الدم وجميع الدهون وانخفاض في وزن الجسم. بعد 10 أيام من العلاج، استطاعت الجرعة 100 ملغ / كغ من المستخلص المائي للبامية الحد بشكل كبير من تأثير ديكساميثازون على الدهون الثلاثية و والليبوبروتين المنخفض الكثافة فقط. ومن ناحية أخري استطاعت الجرعة 200 ملغ / كغ المستخلص المائي للبامية الحد بشكل فعال ومعنوي من تأثير ديكساميثازون على مستويات السكر في الدم والكوليسترول والدهون الثلاثية و والليبوبروتين المنخفض الكثافة. كانت كل الجرعات من المستخلص المائي للبامية قادرة على زيادة تركيز الليبوبروتين العالي الكثافة في الدم.

استنتاج: تشير هذه الدراسة إلى أن المستخلص المائي للبامية يمكن أن يكون مفيدا في الوقاية من ارتفاع السكر وفرط دهون الدم الناجم عن العلاج بـ ديكساميثازون.

الكلمات المفتاحية: أبيلموششوس إسكولنتوس (إ)، فرط سكر الدم، فرط شحميات الدم، ديكساميثازون، البامية.