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Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in *Meriones shawi* rats

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ABSTRACT

Ethnopharmacological relevance: The use of an aqueous extract of coriander (*Coriandrum sativum* L.; Apiaceae, Umbelliferae) seeds (CS-extract) in Moroccan traditional treatment of diabetes remains to be experimentally validated.
Aim of the study: The study aim was to investigate potential hypoglycemic (and hypolipidemic) activity of CS-extract after a single oral dose and after daily dosing for 30 days (sub-chronic study) in normal and obese–hyperglycemic–hyperlipidemic (OHH) *Meriones shawi* rats.
Materials and methods: After a single oral dose of CS-extract (20 mg/kg; predetermined as optimum), plasma glucose, insulin, total cholesterol (TC), and triglycerides (TG) were measured in normal and OHH rats (hypercaloric diet and forced limited physical activity); glibenclamide (GLB; 2.5 mg/kg) was used as reference. In the sub-chronic study, the effect of CS-extract and GLB (at the above doses) on body weight (BW), plasma glucose, insulin, TC, LDL-cholesterol, HDL-cholesterol, TG, urea and creatinine was determined in normal and OHH rats; insulin resistance (IR as HOMA-IR), atherosclerotic and cardioprotective indices were calculated.
Results: A single dose of CS-extract or GLB suppressed hyperglycemia in OHH rats, and normo-glycemia was achieved at 6-h post-dose; there was no effect on lipids, TG or insulin, but IR decreased significantly. The hypoglycemic effect was lower in normal rats. In the sub-chronic study in OHH rats, the test substances (CS-extract > GLB) reduced plasma glucose (normoglycemia on Day 21), insulin and IR, TC, LDL-cholesterol, and TG. Atherosclerotic index decreased while cardioprotective indices increased only by CS-extract, with no effect on BW, urea or creatinine.
Conclusion: Sub-chronic administration of CS-extract in OHH *Meriones shawi* rats normalized glycemia and decreased the elevated levels of insulin, IR, TC, LDL-cholesterol and TG. Since, the CS-extract decreased several components of the metabolic syndrome and decreased atherosclerotic and increased cardioprotective indices, CS-extract may have cardiovascular protective effect. The present study validates the traditional use of coriander in diabetes.

1. Introduction

Diabetes is rapidly becoming a global health crisis. About 97% of diabetics have type 2 diabetes mellitus (T_2DM), and a large proportion of the population is pre-diabetic (with impaired glucose intolerance and insulin resistance; IR) (International Diabetes Federation, 2009). Obesity is becoming an epidemic worldwide; it is associated with a number of pathologies including glucose intolerance, IR, T_2DM and dyslipidemia/hyperlipidemia, all of which are risk factors for CV disease and mortality (Eckel et al., 2004). Obesity accompanied by hyperlipidemia/hyperglycemia, often caused by a lifestyle including overeating and physical inactivity, may lead to metabolic syndrome (Israili et al., 2007), which is a risk factor for CV disease and T_2DM (American Diabetes Association, 2010).

Ideal treatment of diabetes, in addition to effective control of hyperglycemia, should have a favorable effect on dyslipidemia/hyperlipidemia. Most of the presently available antidiabetic drugs do not necessarily have a favorable effect on lipid profile and

Abbreviations: BW, body weight; CS, *Coriandrum sativum*; SEM, standard error of measurement; CV, cardiovascular; GLB, glibenclamide; HDL, High density lipoprotein; HOMA, homeostasis model assessment; IR, insulin resistance; LDL, low density lipoprotein; OHH, obese–hyperglycemic–hyperlipidemic; T_2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides.

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Table 1
Dose optimization: effect of oral administration of a lyophilised aqueous extract of *Coriandrum sativum* seeds (CE-extract) at single doses of 10, 20, 40, 100, 200 and 400 mg/kg BW on plasma levels of glucose, total cholesterol, and triglycerides in OHH *Meriones shawi* rats at 6 h after the dose.

Dose of CE-extract (mg/kg)	Parameter	Plasma concentration (mmol/L)		Effect of dose (%)
		0 h	6 h	
10	Total cholesterol	5.72 ± 0.19	5.69 ± 0.30	−0.52
	Triglycerides	3.11 ± 0.34	2.98 ± 0.35	−8.36
	Glucose	10.28 ± 0.72	8.50 ± 0.80	−7.30
20	Total cholesterol	5.72 ± 0.19	5.59 ± 0.16	−2.27
	Triglycerides	3.11 ± 0.34	2.81 ± 0.32	−9.64
	Glucose	10.28 ± 0.72	6.01 ± 0.51	−41.53
40	Total cholesterol	5.72 ± 0.19	5.59 ± 0.30	−2.27
	Triglycerides	3.11 ± 0.34	2.80 ± 0.35	−9.64
	Glucose	10.28 ± 0.72	6.00 ± 0.75	−41.63
100	Total cholesterol	5.72 ± 0.19	5.70 ± 0.22	−0.35
	Triglycerides	3.11 ± 0.34	2.90 ± 0.36	−6.75
	Glucose	10.28 ± 0.72	6.50 ± 0.60	−36.77
200	Total cholesterol	5.72 ± 0.19	5.65 ± 0.20	−1.22
	Triglycerides	3.11 ± 0.34	2.86 ± 0.32	−8.03
	Glucose	10.28 ± 0.72	6.46 ± 0.68	−37.16
400	Total cholesterol	5.72 ± 0.19	5.65 ± 0.21	−1.22
	Triglycerides	3.11 ± 0.34	2.85 ± 0.32	−8.36
	Glucose	10.28 ± 0.72	6.20 ± 0.70	−39.67

The effect of dose (% change) was calculated as = [value before the dose − value 6 h after the dose]/[value before the dose] × 100; each animal served as its own control (data represent mean ± S.E.M. of 4 rats).

CV risk factors. Therefore, new therapeutic agents, with relatively low adverse drug profile, are needed to control hyperglycemia and also correct dyslipidemia/hyperlipidemia.

Plant medicine is used worldwide in the traditional treatment of many diseases; about 800–1200 plants have been reported to be empirically used in various cultures in the traditional treatment of diabetes. The leaves and the fruits (seeds) of the herb, *Coriandrum sativum* L. (Apiaceae, Umbelliferae, also known as coriander, cilantro, Arab parsley, Chinese parsley, Dhania, etc.), are commonly used in many cuisines. *Coriandrum sativum* is widely used in traditional medicine, for example, in the treatment of digestive disorders, diseases of the respiratory and urinary systems, relief of anxiety and insomnia, in allergies, amoebic dysentery, burns, cough, cystitis, dizziness, edema, hay fever, headache, hemorrhoids, rash, urethritis, urinary tract infection, urticaria, and vomiting (Duke, 1997; Emamghoreishi et al., 2005; PDR-HM, 2007; Aggarwal and Kunnumakkara, 2009).

Locally known as "Kasbour," coriander is used in Morocco in the traditional treatment of various diseases, including diabetes and dyslipidemia (Tahraoui et al., 2007), indigestion, flatulence, insomnia, renal disorders, loss of appetite and as a diuretic (Aissaoui et al., 2008). Pharmacological studies have demonstrated hypoglycemic effect of coriander *in vitro* (Gray and Flatt, 1999), and hypolipidemic (Chithra and Leelamma, 1997), antihypertensive (Jabeen et al., 2009), anti-inflammatory (Zanusso-Junior et al., 2011), anxiolytic (Emamghoreishi et al., 2005), antimicrobial (Kubo et al., 2004; Duman et al., 2010), diuretic (Aissaoui et al., 2008; Jabeen et al., 2009), and cognition improvement (Mani et al., 2011) activity of coriander in experimental animals. The essential oil extracted from coriander seeds is claimed to be a "panacea," beneficial in a wide variety of conditions and diseases (http://www.organicfacts.net/health-benefits/herbs-and-spices/health-benefits-ofcoriander.html; assessed February 2011).

A large number of compounds have been isolated from coriander, including flavonoids (quercetin and isoquercetin), polyphenols (rutin, caffeic acid derivatives, ferrulic acid, gallic acid and chlorogenic acid), β-caroteinoids, anethole, borneol, camphene, camphor, carvone, cineole, citronelol, coriandrol, coriandrin, coumarins and hydroxy-coumarins (umbelliferone and scopoletin), p-cymene, euginol, geraniol, geranyl acetate, limonene, d(+)-linalool, myrcene, α- and β-phellandrene, α- and β-pinenes, α- and γ-terpinene, 5- and 8-methoxypsoralens, tannins, and many others (Ishikawa et al., 2003; Kubo et al., 2004; PDR-HM, 2007).

Since, the hypoglycemic (and hypolipidemic) effect of coriander seed has not been experimentally confirmed *in vivo*, we determined the potential hypoglycemic and hypolipidemic activity of a lyophilized aqueous extract of coriander seeds (CS-extract) after acute and sub-chronic oral administration in *Meriones shawi* rats, which develop obesity, hyperglycemia and hyperlipidemia (OHH), if maintained on a hypercaloric diet and forced limited physical activity (Berrougui et al., 2003; Gaamoussi et al., 2009). The antidiabetic drug, glibenclamide (GLB, glyburide), shown to have hypoglycemic and hypolipidemic effects in animal models of diabetes (Fatima et al., 2010), was used as the reference compound.

2. Materials and methods

2.1. Preparation of the aqueous extract of Coriandrum sativum seeds

The whole plant *Coriandrum sativum* was harvested in the western part of Morocco at the time of maturity of seeds (August and September), and authenticated by Professor M. Fennane of the Scientific National Institute (Rabat, Morocco), and a voucher specimen (C3) was deposited in the herbarium of the Institute.

Coriander seeds were washed well with water, air dried at room temperature and then ground in an electric grinder to have a coarse powder. Fifty grams of the seed powder was suspended in distilled water (500 mL) and heated to boil under reflux for 30 min. The decoction obtained was centrifuged, filtered, frozen at −20 °C and lyophilized (FreeZone® Dry 4.5, USA) to give a residue (yield = 10% w/w). For assuring stability, the residue was stored at −20 °C until used, and CS-extract was prepared in distilled water on the days of experiments. A screening test (dose optimization) was carried out with single doses of 0, 20, 40, 100, 200 and 400 mg/kg of the CE-extract (administered orally to groups of 4 OHH rats at each dose), and the smallest dose (20 mg/kg) giving the best results (lowest glycemia at 6 h after dose) was chosen for this study (Table 1).