HYPOGLYCEMIC EFFECT OF THYMOQUINONE

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SUMMARY

The aim of this study was to investigate the hypoglycemic effect of Thymoquinone in Streptozotocin (STZ)-induced diabetic rats and to elucidate the mechanisms underlying the hypoglycemic effect in terms of hepatic glucose production. Diabetes was induced by intraperitoneal injection of 65 mg/kg body weight of STZ. Treatment with Thymoquinone commenced 4 weeks after induction of diabetes at a dose of 50 mg/kg body weight by gastric gavage. Isolated hepatocytes were collected using collagenase to determine liver glucose production. Thymoquinone reduced blood glucose from 350 ± 4.1 mg/dl before treatment to 262 ± 3.2, 194 ± 3.9 and 184 ± 3.1 mg/dl after 10, 20 and 30 days of treatment, respectively. Hepatic glucose production from gluconeogenic precursors (alanine, glycerol and lactate) was significantly decreased in treated rats. Our data indicated that Thymoquinone possesses hypoglycemic effect in STZ-diabetic rats. The Hypoglycemic effect of Thymoquinone is in part due to a decrease in hepatic gluconeogenesis.

INTRODUCTION

Black seed (Nigella sativa L. Family: Ranunculaceae) is extensively used in traditional medicine, for treatment of various respiratory and gastrointestinal diseases in all the Islamic countries, from Morocco to Pakistan (Riaz et al., 1996) and, locally, in southern Europe. The composition and properties of this species have been investigated (Filippo et al., 2002). Whole seeds or their extracts have antidiabetic, antihistaminic, antihypertensive, anti-inflammatory, antimicrobial, antitumor, galactagogue and insect repellent effects (Riaz et al., 1996; Siddiqui and Sharma 1996; Worthen et al 1998). Most properties are mainly attributed to quinone constituents, of which Thymoquinone (TQ) is the main active constituent of the volatile oil of the black seed and is more abundant compound (Aboutabl et al., 1986). Thymoquinone has been demonstrated to possess strong antioxidant properties (Houghton et al., 1995), and recently has been shown to protect non-tumor tissues from chemotherapy-induced damage (Badary et al., 1997; Al-Shabanah et al., 1998). The pathogenesis of diabetes mellitus and the possible management of
diabetes in animals by oral hypoglycemic agents have been extensively investigated in recent years (Ribes et al., 1986). Although the hypoglycemic effect of Nigella sativa has been investigated in experimentally-induced diabetes in animals (Al-Hader et al., 1993; Deresinski 1995; Fararh et al., 2002), the hypoglycemic effect of Thymoquinone has not been studied yet. Therefore the present study was designed to investigate the hypoglycemic effect of Thymoquinone and its possible mechanism especially with respect to hepatic gluconeogenesis in experimentally-induced diabetic rats.

MATERIAL AND METHODS

Thymoquinone

Thymoquinone was obtained from Sigma Chemical Co. (USA). It was dissolved by initial addition of dimethyl sulfoxide (DMSO), followed by addition of normal saline. Oil was administered at a dose of 50 mg/kg body weight once daily by gastric gavage for one month.

Animals

40 male rats, Eight-week-old (80-120 gm body weight) were placed in stainless steel cages and maintained under suitable lighting, temperature and hygienic conditions. Well-balanced rations and drinking water were provided. Rats were observed for 12 days prior to experimentation. Animals were anesthetized with diethyl ether and then sacrificed by exsanguinations from the carotid arteries. All surgical procedures and pre- and post-operative care of the animals were done in accordance with the standard guidelines and all efforts were made to minimize animal suffering and the number of animals used.

Streptozotocin-induced diabetes:

Streptozotocin (STZ) was obtained from Sigma Chemical Co. (USA). 30 Rats were injected intraperitoneally with a single dose of STZ (65 mg/kg body weight) in a volume of 0.5 ml/rat. STZ was dissolved in sodium citrate buffer solution (pH 4.7; Wako Pure Chemicals, Osaka, Japan) immediately before use. Animals were fasted for 6 hours prior to injection of STZ (Karnieli et al., 1981). Control animals were injected with an equal amount of the buffer solution alone. All animals were then maintained for 4 weeks on ad libitum food and water with monitoring of blood glucose, body weight and food and water consumption before commencement of treatment with Thymoquinone. Animals were divided into 4 equal groups, control normal, diabetic untreated, diabetic