INTRODUCTION

Oxidative stress plays an important role in the etiology of DM (1). Diabetics and experimental animal models exhibit high oxidative stress markers and reactive oxygen species (ROS) in pancreatic islets due to persistent and chronic hyperglycemia, thereby deplete the activity of the antioxidative defense system and thus promote free radical generation (2).

The cellular antioxidant status determines the susceptibility to oxidative damage and is usually altered in response to oxidative stress. Accordingly, interest has recently grown in the role and usage of natural antioxidants as means to prevent oxidative damage in DM with high oxidative stress. The antioxidants such as SOD, CAT and GSHPx are the initial step to protect the cells against lipid peroxidation (3). Reduced antioxidant levels as a result of increased free radical production in experimental DM have been reported (4).

Flavonoids are a group of naturally occurring compounds widely distributed as secondary metabolites in the plants (5). They have been recognized for having interesting clinical properties, such as anti-inflammatory, anti-allergic, anti-viral, anti-bacterial, and anti-tumor activities (6). One of these flavonoids, QE (3,5,7,3',4'-pentahydroxyflavone), prevents oxidant injury and cell death by several mechanisms, such as scavenging oxygen radicals protecting against lipid peroxidation and chelating metal ions (7).

Many scientists studied and are studying plant drugs useful in DM and some of them having antioxidant properties (3, 6, 8,
Due to the presence of aromatic hydroxyl groups, flavonoids have strong antioxidant properties (9). They are scavengers of reactive oxygen and nitrogen species and, therefore, inhibit peroxidation reactions. They, also, protect macrophages from oxidative stress by keeping glutathione in its reduced form (10). Flavonoids have the capacity to inhibit enzymes such as cyclooxygenases and protein kinases involved in cell proliferation and apoptosis (11). They, also, protect normal rat islets from STZ, normalize blood glucose levels and promote cell regeneration in islets of STZ-treated rats (12). Tritiated thymidine incorporation into islet cell DNA was, also, enhanced by these flavonoids in an in vitro study (13). However, the beneficial effects of flavonoids on DNA adduct levels, oxidative damage to DNA and chromosomal aberrations in human could not be demonstrated (14). A different flavonoid, QE, used in doses of 15–50 mg/kg body mass was capable of normalizing blood glucose level, augmenting liver glycogen content and significantly reducing serum cholesterol and LDL concentration in alloxan–diabetic rats (15). Exposure of isolated rat islets to certain flavonoids such as QE enhances insulin release by 44–70% via alteration in calcium fluxes and in cyclic nucleotide metabolism (16).

The present study was undertaken to determine the effect of minimal dose of QE on antioxidant status and blood glucose concentration in normoglycemic and STZ induced diabetic rats.

**MATERIALS AND METHODS**

**Reagents:** QE was obtained from Sigma Chemical Company (USA) and dissolved in 0.5ml of 60% ethanol just before injection. Streptozocin vials containing 1 g streptozocin and 220 mg citric acid was obtained from Upjohn Co. (USA). Streptozocin was reconstituted with 9.5 ml of 0.9% NaCl solution to pH 3.5–4.5 according to manufacturer’s instructions. Furthermore, dilution of the drug was performed in 0.9% NaCl solution immediately before use. The enzymatic kits for the determination of glucose was supplied by (Bicon, Co. Germany).

**Animal experiments:** Adult male albino rats bred and raised at the Assiut University animal quarters with a mass ranging from 200 to 250 g and averaging 16 weeks old were used and maintained at 20-22°C, light period 7.00a.m. to 7.00p.m., and relative humidity 55%. Five animals each were housed in a cage and were given a rat Purina chow diet, water ad libitum. DM was induced by single intraperitoneal injection of streptozocin (50 mg/kg body mass) 3 days after the initiation of treatments. Blood was obtained from the tail vein using heparinized microhematocrit tubes. Plasma glucose of all groups was measured day after day. After one week, glucose tolerance test was done. Animals with plasma glucose level exceeding 16.6 mM were considered as diabetic. All normoglycemic and STZ diabetic rats were employed for the tests described below.

**Effect of quercetin on plasma glucose level:** The required amount of QE was dissolved in 0.5 ml of 60% ethanol prior to injection to rats. Four groups of rats including (five rats per group) were used: (1) normoglycemic control group receiving the vehicle as one intraperitoneal (i.p.) injection of 0.5 ml 60% ethanol per day; (2) normoglycemic rats receiving one i.p. injection of 15 mg QE per kg body mass per day; (3) diabetic control rats receiving one i.p. injection of 0.5 ml 60% ethanol per day; and (4) diabetic experimental animals receiving one i.p. injection of 15 mg QE/kg bw per day. Such treatment was began 3 days prior to induction of DM and continued for 25 days at 13:00 h every day. Blood was collected from the tails using heparinized microhematocrit tubes and used for plasma glucose determination on the day of intraperitoneal injection of STZ (day 0) and every other day thereafter.

**Glucose tolerance test:** Glucose tolerance test was performed according to the procedures of Young et al on the four different groups mentioned above (17). Following QE treatment for 2weeks, plasma glucose was determined, the animals were treated with another respective dose of QE and deprived of food for 24 h. After this period, blood was collected through heparinized tubes for plasma glucose (fasting glucose level). The fasting plasma glucose levels of the all diabetic and control rats groups were done. Fasted animals were fed 1 ml of a glucose solution containing 3 g/kg body weight glucose through a gavage. Tail blood were collected at 45, 90 and 135 min after glucose feeding and plasma glucose levels were determined and used for establishing glucose tolerance curves (17).

**Tissue homogenization and antioxidant enzymes assay:** At killing time (25 days after QE treatment), rats were anaesthetized with sodium pentobarbital (63 mg/kg body weight, intraperitoneally). Blood was collected by cardiac puncture. Pancreas of each rat was removed, cleaned of fatty tissue, blotted dry and weighed. Each pancreas was homogenized in 10 vol. of 50 mM sodium phosphate buffer (pH 7.4) for 30 sec. using a Glas-Col (TURBAX-Germany) homogenizer. The homogenate was filtered through gauze and the filtrate was centrifuged at 1088×g for 5 min in a refrigerated centrifuge. The resultant supernatant was used for measurement of antioxidant enzymes (18).