Diabetes Mellitus and Some Egyptian’s Volatile Oils

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Abstract

Background: Diabetes mellitus as a metabolic disorder is characterized by hyperglycemia, dyslipidemia and deflection in protein metabolism. Natural products as a fashion remedy was undertaken and this study was designed to search the role of anise, fennel, thyme volatile oils and \( \gamma \)-terpinene (a bioactive constituent extracted from caraway and cumin volatile oils) to deal with the biochemical changes in sera, liver and muscle of streptozotocin (STZ)-induced diabetic rats.

Material and methods: Thirty rats (Sprague dawelly) were divided into three groups: control group; diabetic group, STZ-induced diabetic rats and diabetic & volatile oils group. The STZ-induced diabetic & volatile oil group was orally administered with different volatile oils by gavage (2 ml/ kg body weight) and subdivided into four subgroups: diabetic & anise; diabetic & fennel; diabetic & thyme and diabetic & \( \gamma \)-terpinene.

Results: There were highly significant increase in sera glucose, total lipids, total cholesterol, and triglycerides in diabetic rats. Liver and muscle malondialdehyde (MDA) and protein carbonyl (PC), superoxide dismutase, catalase and glutathione-s-transferase activities were remodeling after administration of different volatile oils. Sera insulin, liver glucose-6-phosphate dehydrogenase, liver and muscle glycogen was highly significantly decreased in diabetic rats. On the other hand, the alleviation in these parameters was highly noticed in the different diabetic & volatile oil subgroups.

Conclusion: The counter effects of different volatile oils upon these changes reflect the antihyperglycemia and antioxidant roles of these volatile oils with a different range in STZ-induced diabetic rats.

Key words: Diabetes mellitus, streptozotcin, volatile oils, oxidative stress, antioxidants, glucose metabolism.

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia, dyslipidemia, and protein metabolism that results from defects in both insulin secretion and/or insulin action (Adisakwattana et al., 2005). Activation of multiple metabolic pathways in diabetes leads to increased generation of superoxide and reactive oxygen species (ROS). These include increased mitochondrial electron transport activity that induced by hyperglycemia and fatty acids and enhanced glucose auto-oxidation (Desco et al., 2002). Insulin resistance includes decreased stimulation of muscle glycogen synthesis, defects in glycogen synthesis and hexokinase activity (Muller et al., 1973) and decrease glucose-6-phosphate dehydrogenase (G6PhD) (Wan et al., 2002).

In streptozotocin (STZ) induced type 1 diabetes, hyperglycemia and oxidative stress have been implicated in the etiology and pathology of disease complications (Baynes, 1991). Diabetes mellitus is associated with oxidative stress, leading to an increased production of reactive oxygen species (ROS), including superoxide radical (O2\(^{−}\)), hydrogen peroxide (H\(_2\)O\(_2\)) and hydroxyl radical (OH\(^{−}\)) or impaired and reduction of antioxidant enzyme (Pari and Latha 2004; Vincent et al., 2004; Rahimi et al., 2005). During pathogenesis of diabetes mellitus, oxidative and nitrosative stresses contribute to the destruction of insulin-producing \( \beta \)-cells (Denaly et al., 1997).

Lipid peroxidation (LPO) is a key marker of oxidative stress is a free radical-induced process causing oxidative
deterioration of polyunsaturated fatty acids that eventually results in extensive membrane damage and dysfunction. The significant extent of LPO products that was measured as thiobarbituric acid reactive substances has been reported in diabetes (Rajasekaran et al., 2005). An increased accumulation of the LPO product has been shown in the liver of diabetic rats (Traverso et al., 2002). ROS leading to protein oxidation include radical species such as superoxide (O$_{2}^−$), hydroxyl (OH$^·$), peroxyl (RO$_{2}^·$), alkoxyl (RO$^·$), hydroperoxy (HO$_{2}^·$), and nonradical species such as hydrogen peroxide (H$_2$O$_2$), hypochlorous acid (HOCl), ozone (O$_3$), singlet oxygen (¹O$_2$), and peroxynitrite (ONOO$^−$) (Berlett and Stadtman 1997). The usage of PC groups as biomarkers of oxidative stress has some advantages in comparison with the measurement of other oxidation products because of the relative early formation and the relative stability of carboxylated proteins (Dalle-Donne et al., 2003).

Oxidative stress, arising as a result of an imbalance between free radicals and antioxidant defenses, is associated with damage to lipids, proteins, and nucleic acids, which could contribute to cellular dysfunctions leading to the pathophysiology of various diseases including atherosclerosis, cancer, and diabetes mellitus (Wan et al., 2000). The formation of ROS was prevented by an antioxidant system that included non-enzymatic antioxidants (ascorbic acid, glutathione, tocopherols), enzymes regenerating the reduced forms of antioxidants, and ROS-scavenging enzymes such as superoxide dismutase (SOD), catalase (CAT) (Sarkhail et al., 2007). SOD is one of the important enzymes and scavenges the superoxide radical by converting them to H$_2$O$_2$ and molecular oxygen (Vincent et al., 2004; Lin et al., 2005). The decreased activities of SOD, CAT and glutathione peroxidase (GPx) in liver during diabetes mellitus may be due to the production of ROS such as superoxide (O$_2^−$), hydrogen peroxide (H$_2$O$_2$), and hydroxyl radical (OH$^·$) (Vincent et al., 2004; Kaleem et al., 2006). Moreover, CAT as has been regarded as a major determinant of hepatic antioxidant status and catalyzes the reduction of hydrogen peroxides and protects the tissue from highly reactive hydroxyl radicals (Kaleem et al., 2006).

The glutathione-S-transferases (GSTs) constitute one of the major components of the phase II drug-metabolizing enzyme and antioxidant systems. It appears that GSTs are also regulated both in vivo and in vitro by reactive oxygen species (ROS) such as superoxides, H$_2$O$_2$ and by the products of membrane lipid peroxidation (Mari and Cederbaum, 2001). The GSTs catalyze the conjugation of glutathione to a wide range of electrophiles and represent a protective mechanism against oxidative stress (Ketter, 1998). In STZ-induced diabetic rats, it has also been shown to cause a reduction in the glutathione (GSH)-dependent antioxidant potentials of tissues, thereby making them more susceptible to increased oxidative damage (Baynes and Thorpe, 1999). Tissue-specific altered expression of GST isoenzymes and related catalytic activities in STZ-induced diabetic rats were proved by (Raza et al., 2000). Saito-Yamanaka et al. (1993) found decreased GST activity in the liver of streptozotocin-induced diabetic rats as compared with normal rat livers.

The underlying goal of all diabetes treatment and management is to maintain an adequate blood glucose concentration. Four major classes of oral hypoglycemic agents have been used extensively: insulin secretagogues, biguanides, thiazolidinediones and glucosidase inhibitors (Charpentier, 2002). Each drug class works on different mechanism of actions, including stimulation of insulin secretion, reduction of hepatic gluconeogenesis, increase in insulin receptor sensitivity and delay of digestion and absorption of carbohydrate, respectively. Unfortunately, these agents could produce severe hypoglycemia, weight gain and gastrointestinal disturbances.

Many traditional folk medicinal herb extracts have been used for the treatment of diabetes mellitus. Many extracts showed good free radical scavenging activity. However, most of them have been shown to exert little or no effect on glycemic control in experimental studies, although some herbs possess hypoglycemic properties (Bailey and Day, 1989). Currently, there is growing interest in herbal remedies due to the side effects associated with the therap-
eutic agents (oral hypoglycemic agents and insulin) for the treatment of diabetes mellitus (Kameswara Rao et al., 1997). Natural plant drugs are frequently considered to be less toxic with lower side effects than synthetic ones (Hu et al., 2003; Aliahmadi et al., 2006). Recently, natural products have been explored for antidiabetic activity.

There is an extensive use of essential oils in various domains of human activities such as, aromatherapy, food flavoring fragrances, cosmetics and pharmacy. Anise and fennel essential oils (Pimpinella anisum L., Foeniculum vulgarius M., family Apiaceae) are commonly used as a natural remedy and as ingredients of cosmetic and pharmaceutical products for their balsamic, cardiotonic, digestive, lactogogue and tonic properties (Damjanovic et al., 2005). Hypoglycemic effects have been reported for some plants that contain terpenoids, iridoid glycosides, flavonoids, and other phenolic compounds (Li et al., 2004). In addition, a number of secondary metabolites like flavonoids, phenolic acids, phenylpropanoids, and terpenoids have shown significant antioxidant properties (Harput et al., 2006; Topu et al., 2007).

Material and methods

Chemicals:

Anise (Pimpinella anisum L.) and fennel (Foeniculum vulgarius M.) essential oils are commercially available and were purchased from Harraz Drug stores, Bab El-Khalk, Cairo, Egypt. They were analyzed by (GC) and GC-MS spectrometry (Dawidar et al., 2007). The main components of anise oil were; trans-anethole (61.7%), α-longipinene (10.1%), cis-anethole (7.3%), cyclasativene (5.2%), isoledene (3.4%) and safrol (2.4%), while those of fennel essential oil (EO) were; δ-limonene (34.6%), trans-anethole (13.6%), d-carvone (11%), cis-sabinene hydrate (5.9%), fenchone (3.9%), β-longipinene (2.5%), 1,8-cineol (2.0%) and apiol (1.2%). Thyme (Thymus vulgaris L.) caraway (Carum carvi) and cumin (Cuminum cyminum) essential oils are commercially available in the local Egyptian market. They were also analyzed by (GC) and GC/MS spectrometry and one component of caraway and cumin oils (γ-terpinene, 9.77%) was only used. The chemicals used for chemical analysis were obtained from Sigma, BDH chemicals LTD.

Induction of diabetes:

Diabetes was induced by intravenous injection of streptozotocin (Sigma, St Louis, MO, USA) into the tail vein at a dose of 65 mg/kg body weight. STZ was extemporaneously dissolved in 0.1 M cold sodium citrate buffer, pH 4.5 (Eddoucks et al., 2004). The animals were considered as diabetic, if their blood glucose values were above 250 mg/dl on the 3rd day after STZ injection. The treatment was started on the 4th day after STZ injection and this was considered as 1st day of treatment. The treatment was continued for 7 days.

Animal grouping:

Male albino rats (Sprague dawelly), with an average body weight of 130 to150 g, were purchased from National Research Center, Giza, Egypt. Animals were divided into three groups of five rats per group: control group; diabetic group, STZ-induced diabetic rats and diabetic & volatile oils group. The later one was subdivided into four subgroups: diabetic & anise; diabetic & fennel; diabetic & thyme and diabetic & γ-terpinene. The STZ-induced diabetic & volatile oil subgroups were individually administered with oils by gavage (2 ml/ kg body weight). During four hours of treatment, the animals were housed in steel mesh cage and were given free access to water and a powdered diet. Blood samples were collected from the medial acanthus of the eye for measuring blood glucose levels by One Touch blood glucose meter from life scan. With the end of seventh day, the animals were sacrificed and blood collected and centrifuged at 4000 rpm for 15 min. Sera collected and stored at -20°C for later analysis. The liver and gastrocnemius muscle specimens were cut and homogenized by electrical homogenizer and diluted to 10% in phosphate buffer (pH 7.4).

Methodology:

The concentration of serum glucose was estimated according to the method of Trinder (1969). The concentration of serum insulin was estimated by the method of Yallow and Berson (1959). Liver glycogen
content was determined as described by Nicholas et al., (1956). Glucose-6-phosphate dehydrogenase activity was measured as described by Chan et al., (1965). Protein carbonyl content was measured by first forming labeled protein hydrazone derivatives using 2, 4-dinitrophenyl hydrazine (Smith et al., 1991). The SOD activity of Pancreas and liver homogenates was assayed by the procedure of Niskikimi et al. (1972). Catalase (CAT) activity was measured according to the method of Aebi (1980). Glutathione-s-transferase (GST) activity was determined according to the method of Habig and Jakoby (1981). Lipid peroxidation (MDA) was measured in liver homogenate according to the modification of the method of Ohkawa et al. (1979). Liver total lipids level was estimated according to the method of Frings et al. (1972). The concentration of total cholesterol in serum was estimated method of Young (2001). Serum triglycerides concentration was estimated by method of Fossati and Prencipe (1982).

**Results**

Table (1), serum insulin shows very highly decrease in diabetic rats compared to their control but there is a highly significant hyperglycemia which reflected by highly significant decrease in liver and muscle uptaking of glucose from the blood as there is a decrease in the liver and muscle glycogen content. γ-Terpinene is more efficient than anise, fennel and thyme in alleviation of these changes.

Table (2), shows very highly significant increase in malondialdehyde in both liver and muscle tissues in diabetic rats, but the improvements are highly significant in the active component γ-terpinene than the other volatile oils. On the other hand, liver and muscle total lipids showed very highly significant decrease in diabetic rats but in sera there are highly significant increases in total lipids, total cholesterol and triglycerides levels in diabetic rats. The improvement is pronounced in all treated groups.

In table (3): there is a highly significant increase in liver and muscle protein carbonyl in diabetic group in comparing with control group. There is more alleviation in diabetic & thyme group than in others treated groups.

Table (4): liver and muscle SOD, CAT and GST activities are very highly significant decrease in diabetic rats and all volatile oils and γ-terpinene show high efficient as antioxidant agents.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Diabetes</th>
<th>Diabetes &amp; Anise</th>
<th>Diabetes &amp; Fennel</th>
<th>Diabetes &amp; Thyme</th>
<th>Diabetes &amp; γ-Terpinene</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin</strong></td>
<td>0.85±0.03</td>
<td>0.24±0.02**</td>
<td>0.52±0.01</td>
<td>0.73±0.16</td>
<td>0.45±0.05</td>
<td>0.87±0.01</td>
</tr>
<tr>
<td><strong>Glucose</strong></td>
<td>107.4±5.4</td>
<td>366.6±6.1**</td>
<td>203.0±2.5</td>
<td>228.2±3.4</td>
<td>225.8±1.1</td>
<td>112.0±1.6</td>
</tr>
<tr>
<td><strong>Liver glycogen</strong></td>
<td>661.9±16.7</td>
<td>252.3±2.3</td>
<td>261.9±4.1</td>
<td>329.9±9.5</td>
<td>350.9±4.4</td>
<td>388.6±6.5</td>
</tr>
<tr>
<td><strong>Muscle glycogen</strong></td>
<td>284.6±5.1</td>
<td>97.1±1.6***</td>
<td>133.1±2.0***</td>
<td>184.1±2.8***</td>
<td>193.4±2.7***</td>
<td>198.2±1.3***</td>
</tr>
<tr>
<td><strong>G6phD</strong></td>
<td>3.7±0.05</td>
<td>1.1±0.03***</td>
<td>2.1±0.12***</td>
<td>2.7±0.08***</td>
<td>1.4±0.05***</td>
<td>3.5±0.23***</td>
</tr>
</tbody>
</table>

Mean±SD, P< 0.5 **, P< 0.01 *** and P< 0.001 ***
Table (2) Liver and muscle MDA (nmole/g) and total lipids (mg/g) and serum total lipids (mg/dl), total cholesterol (mg/dl) and triglycerides (mg/dl) in different groups:

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
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<th>Diabetes &amp; γ-Terpinene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver MDA</td>
<td>108.3±6.3</td>
<td>396.9±3.6</td>
<td><strong>310.4±6.5</strong></td>
<td><strong>234.5±3.6</strong></td>
<td>287.3±5.3</td>
<td>125.3±3.1</td>
</tr>
<tr>
<td>Muscle MDA</td>
<td>85.9±4.2</td>
<td>189.6±2.1</td>
<td><strong>118.6±1.8</strong></td>
<td><strong>139.6±1.6</strong></td>
<td>79.8±2.1</td>
<td>62.5±1.4</td>
</tr>
<tr>
<td>Liver total lipids</td>
<td>591.1±1.5</td>
<td>355.2±1.6</td>
<td><strong>442.2±2.1</strong></td>
<td><strong>486.8±2.2</strong></td>
<td>344.2±1.5</td>
<td>445.3±7.4</td>
</tr>
<tr>
<td>Muscle total lipids</td>
<td>551.1±0.9</td>
<td>361.8±1.7</td>
<td><strong>481.2±2.2</strong></td>
<td><strong>488.2±1.8</strong></td>
<td>464.9±2.5</td>
<td>435.5±1.5</td>
</tr>
<tr>
<td>Serum total lipids</td>
<td>444.9±3.8</td>
<td>524.7±4.2</td>
<td><strong>372.7±1.9</strong></td>
<td><strong>365.9±8.8</strong></td>
<td>342.2±3.3</td>
<td>377.4±2.3</td>
</tr>
<tr>
<td>Serum total cholesterol</td>
<td>71.3±1.2</td>
<td>176.3±1.5</td>
<td><strong>71.9±0.92</strong></td>
<td><strong>100.4±1.1</strong></td>
<td>105.2±1.7</td>
<td>83.2±1.5</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>205.6±1.5</td>
<td>265.2±4.5</td>
<td><strong>257.6±2.2</strong></td>
<td><strong>247.2±1.5</strong></td>
<td>246.8±2.5</td>
<td>234.3±2.6</td>
</tr>
</tbody>
</table>

Mean±SD, P< 0.5 *, P< 0.01 ** and P< 0.001 ***

Table (3) Liver and muscle protein carbonyl (µmol/g) and total protein contents (mg/g) in different groups:

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Diabetes</th>
<th>Diabetes &amp; Anise</th>
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<th>Diabetes &amp; Thyme</th>
<th>Diabetes &amp; γ-Terpinene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver PC</td>
<td>60.3±1.11</td>
<td>146.1±1.5</td>
<td><strong>124.8±2.3</strong></td>
<td><strong>107.5±2.5</strong></td>
<td>75.1±1.5</td>
<td>120.3±3.2</td>
</tr>
<tr>
<td>Muscle PC</td>
<td>91.2±1.6</td>
<td>204.8±3.6</td>
<td><strong>154.8±1.9</strong></td>
<td><strong>128.7±3.9</strong></td>
<td>112.3±2.2</td>
<td>123.0±6.19</td>
</tr>
<tr>
<td>Liver total protein</td>
<td>10.1±0.78</td>
<td>8.4±0.44</td>
<td><strong>13.2±1.9</strong></td>
<td><strong>9.0±0.1</strong></td>
<td>9.8±0.47</td>
<td>10.6±0.45</td>
</tr>
<tr>
<td>Muscle total protein</td>
<td>10.7±0.66</td>
<td>7.7±0.16</td>
<td><strong>8.2±0.12</strong></td>
<td><strong>7.5±0.15</strong></td>
<td>8.4±0.26</td>
<td>7.3±0.16</td>
</tr>
</tbody>
</table>

Mean±SD, P< 0.5 *, P< 0.01 ** and P< 0.001 ***

Table (4): Liver and muscle SOD (U/mg), CAT (U/mg) and GST (U/sec/mg) activities in different groups:

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Diabetes</th>
<th>Diabetes &amp; Anise</th>
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<th>Diabetes &amp; Thyme</th>
<th>Diabetes &amp; γ-Terpinene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver SOD</td>
<td>16.5±0.3</td>
<td>14.3±0.2</td>
<td><strong>16.6±0.3</strong></td>
<td><strong>11.4±0.3</strong></td>
<td>15.2±0.2</td>
<td>15.5±0.2</td>
</tr>
<tr>
<td>Muscle SOD</td>
<td>13.9±0.2</td>
<td>8.6±0.2</td>
<td><strong>12.7±0.2</strong></td>
<td><strong>11.7±0.5</strong></td>
<td>10.6±0.3</td>
<td>11.9±0.4</td>
</tr>
<tr>
<td>Liver CAT</td>
<td>1.4±0.1</td>
<td>0.35±0.02</td>
<td><strong>0.48±0.02</strong></td>
<td><strong>0.89±0.01</strong></td>
<td>0.67±0.02</td>
<td>1.3±0.1</td>
</tr>
<tr>
<td>Muscle CAT</td>
<td>0.77±0.02</td>
<td>0.37±0.02</td>
<td><strong>0.82±0.01</strong></td>
<td><strong>0.63±0.4</strong></td>
<td>0.48±0.01</td>
<td>0.72±0.4</td>
</tr>
<tr>
<td>Liver GST</td>
<td>1.3±0.07</td>
<td>0.19±0.02</td>
<td><strong>0.31±0.02</strong></td>
<td><strong>0.44±0.02</strong></td>
<td>0.95±0.03</td>
<td>0.36±0.2</td>
</tr>
<tr>
<td>Muscle GST</td>
<td>1.8±0.04</td>
<td>0.36±0.02</td>
<td><strong>0.3±0.02</strong></td>
<td><strong>0.25±0.2</strong></td>
<td>0.93±0.04</td>
<td>0.19±0.01</td>
</tr>
</tbody>
</table>

Mean±SD, P< 0.5 *, P< 0.01 ** and P< 0.001 ***
Diabetes Mellitus and Some Egyptian’s Volatile Oils

Discussion

Reactive oxygen and nitrogen species are highly reactive and potentially damaging transient species (characterized by the presence of unpaired electrons) formed in all tissues during normal aerobic cellular metabolism (e.g. via leakage of electrons from mitochondria) (Cheeseman and Slater, 1993) and are formed also in higher fluxes under pathological conditions such as diabetes. In STZ-induced diabetic rats there was an increase in lipid peroxidation and an indirect evidence of intensified free radical production (Maritim et al., 2003). Most of the tissue damage is consider to be mediated by the free radicals and ROS by attacking membranes through peroxidation of unsaturated fatty acids (Stringer et al., 1989). Also, an observed increase in the pancreas level of thiobarbituric acid reactive substances (MDA) may be due to increased susceptibility of the tissue of diabetic rats to lipid peroxidation (Matkovics et al., 1998). In STZ-induced diabetes, oxidative stress contributes to the destruction of insulin-producing β-cells, (Denaly et al., 1997) and this logically explains the acute shortage of plasma insulin level and a significant hyperglycemia in diabetic rats. It is well documented that there is an elevation of serum lipids concentration in diabetics (Chase and Glasgow, 1976). The increase in serum total lipids, triglycerides, total cholesterol levels, due to the increase of liver and muscle lipid peroxidation, decrease insulin-stimulated glucose uptake in the whole body, mainly in the muscle and liver which impair insulin mediated suppression of endogenous glucose production, mainly from the liver (Nakahara et al., 2004), decrease liver G6PhD level (Wan et al., 2002) and impairs hepatic glucose uptake that can lead to metabolic derangement in diabetic rats. A significant hyperglycemia; enhanced glucose auto-oxidation (Desco et al., 2002) and insulin resistance includes decreased stimulation of muscle glycogen synthesis, all of these defect glycogen synthesis (Muller et al., 1973). The decrease in liver and muscle glycogen contents may be interpreted by a decrease in liver glucose-6-dehydrogenase(Wan et al., 2002) which attacked and inhibited by ROS in diabetic rats. The present findings indicate significantly increased lipid peroxidation in liver and muscle of STZ induced diabetic rats and its attenuation by different volatile oils treatment especially with γ-terpinene and fennel. This suggests a protective role of volatile oils and bioactive γ-terpinene which act as strong superoxide radical and singlet oxygen catchers.

On the other hand, Reactive oxygen and nitrogen species cause cellular damage, an important part of which is the oxidation of amino acid residues on proteins, forming protein carbonyls (Chevion et al., 2000). Moreover, The PC may be introduced into proteins by secondary reaction of the nucleophilic side chains of cystiene, histidine, and lysine residues, with malondialdehyde (Dalle-Donne et al., 2003). In diabetic rats, liver and muscle PC contents (arguably of equal importance as lipid peroxidation) were significantly increased and which reflect the decrease in total proteins in both investigated tissues. These changes were alleviated after administration of different VOs especially in thyme volatile oil and γ-terpinene groups. Administration of medicinal plant extract to mildly STZ-diabetic rats resulted in activation of β-cells and returns to normal giving insulinogenic effect (Padmini and Chakrabarti, 1982). Volatile oils may bring about its hypoglycemic action through stimulation of surviving β-cells of islets of langerhans to release more insulin. A number of other plants have also been observed to exert hypoglycemic activity through insulin-release stimulatory effects (Pari and Uma Maheswari, 2000; Prince and Menon, 2000). Some bioactive compounds isolated from plants like terpenoids and flavonoids were reported to affect pancreatic β-cells and stimulate insulin secretion with numerous mechanisms such as exertion distal to K⁺-ATP channels and L-type Ca²⁺ channels (Hoa et al., 2007), activation of the cAMP/PKA signaling (Liu et al., 2006), and antioxidant activities (Waltner et al., 2002; Elmali et al., 2004). Since oxidative stress and free radicals injure or destroy pancreatic β-cells in
diabetes, so volatile oils are able to increase the secretion of insulin via its antioxidant actions.

Cells are protected from ROS induced damage by a variety of endogenous ROS scavenging proteins, enzymes and chemical compounds (Cheeseman and Slater 1993). Numerous studies have revealed lowered antioxidant and enhanced peroxidative status in diabetes mellitus. Insulin deficiency promotes the β-oxidation of fatty acids with resulting H$_2$O$_2$ formation (Horie et al., 1981). Antioxidant enzymes (SOD, CAT) have been shown an important role in maintaining physiological levels of oxygen and hydrogen peroxide by hastening the dismutation of oxygen radicals and eliminating organic peroxides and hydroperoxides generated from inadvertent exposure to STZ (Pari and Latha 2004). The present data well indicate that STZ-induced diabetes disrupts actions of hepatic and muscular antioxidant enzymes (Zhang and Tan 2002). These observations emphasis the critical importance of maintaining the antioxidant potential of pancreatic β-cells in order to ensure both its survival and insulin secretion capacity during times of increased oxidation stress. The decreased activities of SOD and CAT in liver during diabetes mellitus may be due to the production of ROS (Vincent et al., 2004; Kaleem et al., 2006). The observed decrease in SOD activity in diabetic control rats could result from inactivation by H$_2$O$_2$ or by glycosylation of the enzyme, which have been reported to occur in diabetes (Soon and Tan 2002; Ravi et al., 2004). CAT is involved in the elimination of high concentration of H$_2$O$_2$ and it has been regarded as a major determinant of hepatic antioxidant status and catalyzes the reduction of hydrogen peroxides and protects the tissue from highly reactive hydroxyl radicals. Decrease in CAT activity could result from inactivation by superoxide radical and glycation of the enzyme (Rajasekaran et al., 2005).

A reduced GST dependent detoxification of toxic metabolites accompanied by an increased production of ROS, during aerobic glycolysis and increased membrane LPO would, therefore, have serious consequences for cellular functions in the tissues in diabetes, so GSTs may offer protection against diabetes mellitus. Raza et al., (2004) have reported hyperglycemia and glutathione-associated oxidative stress in rats one week after treatment with STZ. In this study lower levels of hepatic antioxidant enzymes and increased LPO in diabetic groups were observed when compared with normal control meanwhile oral administration with volatile oils partially reduced the imbalance between the generations of ROS and scavenging enzymes activity in diabetic rats. As mentioned above, this effect of VOs also backs to existence of terpenoids, iridoid glycosides, flavonoids and related phenolic compounds in it (Li et al., 2004), as well-known antioxidants (Rahimi et al., 2005; Harput et al., 2006; Topu et al., 2007), which scavenge the free radicals and other ROS generated during diabetes.

**Conclusion**

In conclusion, the present study showed that anise, thyme and fennel volatile oils and γ-terpinene have double effects which are beneficial in the controlling of diabetes disorders because they have insulinogenic action on β-cells and reduce the insulin resistance of cells especially for liver and muscle cells, also combating oxidative stress by scavenging the ROS and activation of hepatic and muscular antioxidant enzymes.

**References**


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تأثير بعض الزيوت الطيارة المصرية على مرض السكر المستحث بمادة الستربوتوزوتسين في الجواد

يهدف البحث لدراسة تأثير بعض الزيوت الطيارة المصرية مثل البنسون و الزعتر و الشعر و أيضا مادة الجاما تيربين المستخلصة من زيت الكمون و
Diabetes Mellitus and Some Egyptian’s Volatile Oils

The current study used the diabetic rats of the adult age and which feed in the average weight of 140 g daily. We divided the groups as follows:

1. The control group: fed the same diet without treatment.
2. The control group + sesame oil (55 mg/kg) and in the third day, the diabetic rats were treated with the sesame oil in a dose ranging from 250 mg/kg to 100 mg/kg.
3. The treatment group + the same diet and the treatment with the sesame oil.

The study results showed that the diabetic rats fed with the sesame oil and treated with the sesame oil in doses ranging from 250 mg/kg to 100 mg/kg had a significant increase in the levels of SOD and CAT enzymes compared to the control group. Additionally, the results showed a significant decrease in the levels of GST enzymes in the treatment group compared to the control group. The study also showed that the use of sesame oil in the treatment of diabetes is effective in increasing the levels of antioxidant enzymes and reducing the levels of GST enzymes.