Effect of *Nigella sativa* Tea in Type 2-Diabetic Patients as Regards Glucose Homeostasis, Liver and Kidney Functions

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**ABSTRACT**

**Objective:** The aim of this work was to study the effect of *Nigella sativa* (*N. sativa*) as co-drug in the treatment of type 2 diabetes mellitus (T2DM). **Subjects and Methods:** The present work comprises two groups of subjects matched in age. The first group includes 41 type 2 diabetic patients and the second group includes 25 apparently healthy volunteers identical in age and culture. All subjects received *N. sativa* tea (hot water extract) as 5gm/day for 6 months. The patients were chosen to be free of diabetic complications. They were receiving their oral antidiabetic drug (OAD) in addition to *N. sativa* tea treatment. All subjects were submitted to the following laboratory investigations (using colorimetric methods): 1- Fasting (FBG) and postprandial (PPBG) blood glucose. 2- Glycosylated hemoglobin (HbA1c). 3- Liver functions tests [aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum total, direct and indirect bilirubin]. 4- Kidney functions tests (blood urea and serum creatinine). **Results:** The laboratory investigations of diabetic subjects treated with *N. sativa* tea showed the following results: FBG, PPBG and HbA1c recorded a very highly significant decrease. AST and ALT recorded a significant decrease. Total serum bilirubin showed a very highly significant decrease. Indirect serum bilirubin recorded a significant decrease. Blood urea recorded a very highly significant decrease. Serum creatinine showed a significant decrease in case of both the normal and diabetic groups. **Conclusion:** *N. sativa* tea can be used as co-atidiabetic drug or drug as, the level of blood glucose in patients was decreased clearly and three of our patients stopped the antidiabetic drug as a result of decrease in blood glucose to the normal level.

**Key words:** *Nigella sativa*, Diabetes mellitus, Type 2 diabetes mellitus

**Introduction**

Diabetes mellitus (DM) is a metabolic disorder resulting from a defect in insulin secretion and/or insulin action, which results in hyperglycemia with disturbances of carbohydrate, fat and protein metabolism (Heydari *et al*., 2010). Such a deficiency along with other mechanisms can damage many of the body’s systems. DM is notorious not only for its adverse effects on various metabolic pathways of the body, but also for its tendency to produce various micro (neuropathy, nephropathy and retinopathy) and macrovascular complications (Agrawal *et al*., 2011). Type 2 diabetes mellitus (T2DM) results from an interaction between a genetic predisposition and environmental factors. It accounts for around 90% of all cases of DM (Reimann *et al*., 2009).

Type 2 diabetes mellitus is a multifactorial disease, associated with a number of microvascular and macrovascular complications (Heydari *et al*., 2010). These complications include incipient nephropathy. It usually occurs after 6–15 years of DM (Fraser and Phillips, 2007). Even when diabetes is controlled, the disease can lead to chronic kidney disease (CKD) and kidney failure. However, most people with diabetes do not develop severe enough renal dysfunction to progress to kidney failure (Karnib and Ziyadeh, 2010). DM can also affect liver functions as serum concentration of unconjugated and of conjugated bilirubin was increased 1.6 and 8 fold respectively (Gonzalez and Fevery, 1992). Also, normally serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels are low, but these enzymes are released into circulation after cellular damage and increased because they are cytoplasmic in location (Al-Kubaisy and Al-Noaemi, 2007).

Management of T2DM involves controlling weight and optimizing levels of blood glucose, blood pressure, lipids and thereby reducing cardiovascular risk. Pharmacotherapy is almost always required (Dinneen, 2007). Glycaemic control in patients with T2DM is usually assessed by the measurements of the three following markers: glycosylated hemoglobin (HbA1c), fasting plasma glucose (FPG) and postprandial glucose (PPBG)
Two primary techniques are available for health providers and patients to assess the effectiveness of the management plan on glycemic control: patient self-monitoring of blood glucose (SMBG) and A1C measurement (American Diabetes Association, 2008). In addition, many pharmacologic approaches are used in the management of T2DM such as insulin therapy, Insulin Secretagogues (Sulfonylureas, Nonsulfonylurea Insulin Secretagogues and Incretin-Based Insulin Secretagogues), Insulin Sensitizers (Biguanides and Thiazolidinediones) and other medications such as α-Glucosidase Inhibitors, Inhaled insulin, Incretin mimetics and Pramlintide (Karnib and Ziyadeh, 2010).

The use of plants as medicines dates from the earliest years of man’s evolution. Medicinal plants serve as therapeutic alternatives, safer choices, or in some cases, as the only effective treatment (Salem, 2005). Traditionally Nigella sativa (N. sativa) plant has been in use in many Middle Eastern countries as a natural remedy for DM. Significant reduction in blood glucose level in humans following the use of the plant was reported by Bamosa et al., 2010. This hypoglycemic effect of N. sativa can happen whether it is used as oil (Haq et al., 1999), powder (El-Naggar and El-Deib, 1992) or even in a plant mixture (Al-Awadi et al., 1991; Eskander et al., 1995; El-Shabrawy and Nada, 1996). N. sativa was also found to have a hepatoprotective effect in diabetic patients by decreasing the elevated AST and ALT levels (El-Shamy et al., 2000). Alcoholic extract or the whole powdered seeds of N. sativa can reduce serum creatinine levels (Al-Okbi et al., 1997). Sayed–Ahmed and Nagi, 2007, suggested that N. sativa can prevent the development of renal failure by a mechanism related, at least in part, to its ability to decrease oxidative stress and to preserve the activity of the anti-oxidant enzymes, as well as, its ability to prevent the energy decline in kidney tissue.

Because of the lack of studies or available literatures, the present study aimed to evaluate the antidiabetic effect of N. sativa tea (hot water extract) as co-drug or drug treatment in T2DM.

Subjects and Methods:

Subjects:

The present work comprises two groups of subjects matched in age. The first group includes 41 type 2 diabetic patients and the second group includes 25 apparently healthy non diabetic volunteers identical in age and culture.

a- Patients:

The patients group included 41 patients with T2DM. They were recruited from diabetic patients on regular follow-up visits to the NRC out patients’ clinics and Ain Shams Specialized Hospital. DM was diagnosed according to the 1980 World Health Organization Expert Committee Report (WHO, 1980). The patients were chosen to be free of diabetic complications.

b- Healthy subjects:

This group included 25 apparently healthy non-diabetic volunteers.

All subjects consented in advance about the nature of the study and underwent through medical work up.

All subjects received N. sativa tea that was prepared as following:

Mature N. sativa seeds were purchased from the Egyptian agriculture ministry and packed at Atos Pharma factory in filter packs. Each pack contained 2.5 grams of N. sativa seeds.

Every individual of subjects received two packs daily for 6 months. Patients group received their oral antidiabetic drug (OAD) in addition to N. sativa tea.

All subjects were submitted to the following laboratory investigations: 1- Fasting (FBG) and postprandial (PPBG) blood glucose. 2- Glycosylated hemoglobin (HbA1c). 3- Liver functions tests [aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum total, direct and indirect bilirubin]. 4- Kidney functions tests (serum creatinine and blood urea).

Blood sampling:

Blood samples were collected from the subjects in the morning after an overnight fast. 5 ml of venous blood were collected using a sterile plastic syringe monthly for six months. 1 ml of venous blood was added to EDTA in a clean dry test tube to separate plasma. The EDTA-plasma has been used for HbA1c determination. To obtain serum, the other 4 ml of venous blood were left in a dry centrifuge tube for 2 hours in room temperature to clot. Serum was obtained by centrifugation at 4000 r.p.m. for 15 min. at room temperature. 1ml of serum was taken immediately after separation for the measurement of FBG. The rest of serum was divided into 2 clean dry epinorph tubes, one for liver functions, the second for kidney functions. All samples were
stored at -20ºC. After two hours of having breakfast for all the subjects, 1 ml of blood was collected for the measurement of PPBG.

Laboratory investigations:

1- Blood glucose was determined according to the enzymatic colorimetric method of Trinder (1969) using Biodiagnostic Kit, Egypt.
2- Quantitative colorimetric determination of glycohemoglobin (HbA1c) in whole blood was determined as described by Abraham et al (1978) using Stanbio Laboratory kits, Boerne, Texas.
3- Liver functions tests [colorimetric determination of AST and ALT were performed according to Reitman and Frankel (1957) using Biodiagnostic Kit, Egypt. Bilirubin was determined as described by Walters and Gerade (1970) using Biodiagnostic Kit, Egypt.
4- Kidney functions tests (The blood urea was determined according to the Urease-Berthelot Method of Fawcett and Soctt (1960) using Biodiagnostic Kit, Egypt. Quantitative colorimetric determination of creatinine in serum was determined as described by Folin and Wu (1919) using Stanbio Laboratory kits, Boerne, Texas).

Statistical Analysis:

All statistics are performed using SPSS 7.5 for Windows package (SPSS Inc., Chicago, IL, USA). The difference between groups was calculated using T-Test (Paired-Sample T-Test) and the data obtained in the present work are represented in tables as average (mean) ± standard deviation.

Results:

Comparing the values of FBG with that before treatment in both groups, statistical analysis showed a very highly significant decrease ($p<0.001$) in FBG, in case of the normal control group treated with *N. sativa* tea, after 3 and 6 months of treatment. However, there was a significant ($p<0.05$) decrease after one month and a highly significant decrease ($p<0.01$) after two months of treatment. Meanwhile there was a very highly significant ($p<0.001$) decrease of FBG in case of the diabetic patients treated with *N. sativa* tea, after 2, 3 and 6 months of treatment (Table 1 and Fig. 1). Data illustrated in Table 1 and Fig. 2 indicated that there was a very highly significant ($p<0.001$) decrease in PPBG in normal control and diabetic groups treated with *N. sativa* tea as compared to the value before treatment after all time intervals. Statistical analysis showed decreased values of HbA1c when compared to the HbA1c value before treatment after all time intervals. Statistical analysis showed decreased values of HbA1c when compared to the HbA1c value before treatment in both normal control and diabetic groups treated with *N. sativa* tea at both time intervals. This decrease was very highly significant ($p<0.001$) and time-dependant in both groups (Table 1 and Fig. 3).

Statistical analysis, showed a highly significant ($p<0.01$) decrease of AST activity in case of the normal control group after one month and a significant decrease ($p<0.05$) after six months of treatment with *N. sativa* tea. However a non-significant ($p>0.05$) decrease of AST activity after 2 and 3 months of *N. sativa* tea treatment was recorded, while there was a non-significant ($p>0.05$) decrease of the enzyme activity in case of the diabetic group nearly at all time intervals (Table 2 and Fig. 4).

The activity of ALT showed a non-significant ($p>0.05$) decrease in case of the diabetic group treated with *N. sativa* tea, compared to its activity before treatment after all time intervals. However, a very highly significant ($p<0.001$) decrease of ALT activity was recorded in case of the normal control group after 1, 2, 3 and 6 months of treatment with *N. sativa* tea (Table 2 and Fig. 5).

Serum total bilirubin (T. bilirubin) mean level (mg/dl) of both the normal subjects and diabetic patients showed a time-dependant decrease that was statistically very highly significant ($p<0.001$) after six months of treatment (Table 3 and Fig. 6) nearly at all time intervals.

The mean value (mg/dl) of direct bilirubin (D. bilirubin) of the normal group treated with *N. sativa* tea for six months decreased significantly, this decrease was very highly significant ($p<0.001$) after the 1st and 6th months and highly significant ($p<0.01$) after the 2nd and 3rd months. On the other hand, the mean value (mg/dl) of d. bilirubin of the diabetic group was apparently not affected by *N. sativa* tea treatment for six months. Non-significant decrease was recorded at all time intervals except after 2 months that recorded a highly significant ($p<0.01$) decrease (Table 3 and Fig. 7).

The mean level (mg/dl) of indirect bilirubin (I. bilirubin) of normal non-diabetic group was illustrated in Table 3 and Fig. 8. After six months of treatment, the statistical analysis showed a significant ($p<0.05$) decrease. However, there was a progressive and time-dependant decrease in I. bilirubin of diabetic group that was very highly significant ($p<0.001$) after six months of treatment with *N. sativa* tea (Table 3 and Fig. 8).

The mean values (mg/dl)±S.D. of blood urea of the normal non diabetic group and that of diabetic patients before and after treatment with *N. sativa* tea are represented in Table 4 and Fig. 9. A very highly significant
(p≤0.001) decrease of blood urea level was recorded in both the normal control and diabetic groups treated with *N. sativa* tea for six months when compared with the mean value before treatment, at all time intervals.

Comparing with creatinine mean values (mg/dl) before treatment in both groups, statistical analysis showed a significant (p≤0.05) decrease of serum creatinine in case of the normal control group treated with *N. sativa* tea after the 1st and 3rd months, meanwhile there was a non-significant (P≥0.05) decrease after the 2nd month and a very highly significant (p≤0.001) decrease after the 6th month of treatment. On the other hand, a progressive and time-dependant decrease in serum creatinine was recorded in case of the diabetic group treated with *N. sativa* tea (Table 4 and Fig.10) that was highly significant (p≤0.01) after six months of treatment.

**Table 1:** Effect of *Nigella sativa* tea daily treatment (5gm/day) on fasting (FBG) and postprandial (PPBG) blood glucose levels (mg/dl) and glycosylated hemoglobin (HbA1c) % in normal control subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.

<table>
<thead>
<tr>
<th>Time Group</th>
<th>Param.</th>
<th>Before</th>
<th>After one month</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After two months</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After three months</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After six months</th>
<th>T.V.</th>
<th>P.V.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>FBG</td>
<td>80.22 ± 10.8</td>
<td>78.14 ± 10.3</td>
<td>2.30</td>
<td>0.03</td>
<td>0</td>
<td>76.79 ± 8.66</td>
<td>3.50</td>
<td>0.00</td>
<td>2</td>
<td>75.30 ± 8.97</td>
<td>5.00</td>
<td>0.00</td>
<td>73.34 ± 8.71</td>
</tr>
<tr>
<td></td>
<td>PPBG</td>
<td>101.1 ± 15.25</td>
<td>96.01 ± 14.12</td>
<td>5.06</td>
<td>0.00</td>
<td>0</td>
<td>93.16 ± 12.93</td>
<td>7.75</td>
<td>0.00</td>
<td>0</td>
<td>92.20 ± 13.58</td>
<td>8.94</td>
<td>0.00</td>
<td>89.49 ± 12.38</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>4.43 ± 0.36</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4.26 ± 0.51</td>
<td>2.05</td>
<td>0.05</td>
<td>4.14 ± 0.47</td>
</tr>
<tr>
<td>Diabetic</td>
<td>FBG</td>
<td>148.7 ± 26.59</td>
<td>137.9 ± 28.36</td>
<td>5.86</td>
<td>0.00</td>
<td>0</td>
<td>131.6 ± 26.33</td>
<td>7.90</td>
<td>0.00</td>
<td>0</td>
<td>126.4 ± 23.14</td>
<td>9.88</td>
<td>0.00</td>
<td>127.6 ± 22.01</td>
</tr>
<tr>
<td></td>
<td>PPBG</td>
<td>251.4 ± 76.88</td>
<td>216.3 ± 61.09</td>
<td>6.82</td>
<td>0.00</td>
<td>0</td>
<td>192.8 ± 46.11</td>
<td>8.94</td>
<td>0.00</td>
<td>0</td>
<td>174.2 ± 36.60</td>
<td>10.3</td>
<td>0.00</td>
<td>164.1 ± 28.72</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>7.18 ± 0.83</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6.59 ± 0.62</td>
<td>10.5</td>
<td>0.00</td>
<td>6.02 ± 0.58</td>
</tr>
</tbody>
</table>

Data are expressed as Mean±S.D. 
(P≥0.05): insignificant 
(P<0.05): significant 
(P<0.01): highly significant 
(P<0.001): very highly significant

**FBG**

**Fig 1:** Effect of *Nigella sativa* tea daily treatment (5gm/day) on fasting blood glucose (FBG) level (mg/dl) in normal control subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.
Fig. 2: Effect of *Nigella sativa* tea daily treatment (5gm/day) on postprandial blood glucose (PPBG) level (mg/dl) in normal control subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.

HbA1c

Fig. 3: Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum glycosylated hemoglobin (HbA1c) level (%) in normal control subjects and diabetic patients after 3 & 6 months of treatment.

Table 2: Effect of *Nigella sativa* tea daily treatment (5gm/day) on aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels (units/ml) in normal control subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.

<table>
<thead>
<tr>
<th>Time Group</th>
<th>Parameter</th>
<th>Before</th>
<th>After one month</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After two months</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After three months</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After six months</th>
<th>T.V.</th>
<th>P.V.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>AST</td>
<td>22.84 ± 5.03</td>
<td>21.12 ± 5.58</td>
<td>2.93</td>
<td>0.00</td>
<td>22.40 ± 5.33</td>
<td>0.57</td>
<td>0.57</td>
<td>22.60 ± 4.42</td>
<td>0.35</td>
<td>0.73</td>
<td>22.08 ± 5.02</td>
<td>2.28</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>ALT</td>
<td>24.76 ± 7.37</td>
<td>22.64 ± 7.19</td>
<td>3.10</td>
<td>0.00</td>
<td>22.92 ± 6.60</td>
<td>4.72</td>
<td>0.00</td>
<td>22.52 ± 6.95</td>
<td>5.32</td>
<td>0.00</td>
<td>23.24 ± 7.29</td>
<td>4.72</td>
<td>0.000</td>
</tr>
<tr>
<td>Diabetic</td>
<td>AST</td>
<td>28.88 ± 5.07</td>
<td>29.76 ± 4.11</td>
<td>-</td>
<td>-</td>
<td>31.05 ± 5.86</td>
<td>-</td>
<td>-</td>
<td>29.88 ± 4.10</td>
<td>-</td>
<td>-</td>
<td>27.93 ± 4.27</td>
<td>1.26</td>
<td>0.216</td>
</tr>
<tr>
<td></td>
<td>ALT</td>
<td>27.98 ± 5.36</td>
<td>27.24 ± 4.83</td>
<td>1.36</td>
<td>0.18</td>
<td>27.66 ± 4.58</td>
<td>0.47</td>
<td>0.64</td>
<td>27.98 ± 4.52</td>
<td>0.00</td>
<td>1.00</td>
<td>26.83 ± 3.80</td>
<td>1.54</td>
<td>0.132</td>
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</tbody>
</table>

Data are expressed as Mean±S.D.  
*(P≤0.05): significant  
(P≤0.01): highly significant  
(P≤0.001): very highly significant  
(P≥0.05): insignificant*
Fig. 4: Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum aspartate aminotransferase (AST) level (units/ml) in normal control subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.

Fig. 5: Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum alanine aminotransferase (ALT) level (units/ml) in normal control subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.

Table 3: Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum total, direct and indirect bilirubin levels (mg/dl) in normal subjects and diabetic patients after 1, 2, 3 & 6 months of treatment.

<table>
<thead>
<tr>
<th>Time Group</th>
<th>Parameter</th>
<th>Before</th>
<th>After one month</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After two months</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After three months</th>
<th>T.V.</th>
<th>P.V.</th>
<th>After six months</th>
<th>T.V.</th>
<th>P.V.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norma l</td>
<td>T. bilirubin</td>
<td>0.79 ± 0.11</td>
<td>0.76 ± 0.11</td>
<td>4.523</td>
<td>0.00</td>
<td>0.76 ± 0.12</td>
<td>3.58</td>
<td>0.00</td>
<td>0.75 ± 0.12</td>
<td>4.37</td>
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<td>0.76 ± 0.11</td>
<td>4.42</td>
<td>0.00</td>
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<tr>
<td></td>
<td>D. bilirubin</td>
<td>0.17 ± 0.47</td>
<td>0.16 ± 0.40</td>
<td>4.993</td>
<td>0.00</td>
<td>0.16 ± 0.39</td>
<td>3.02</td>
<td>0.00</td>
<td>0.16 ± 0.37</td>
<td>2.86</td>
<td>0.00</td>
<td>0.16 ± 0.44</td>
<td>5.28</td>
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<tr>
<td></td>
<td>I. bilirubin</td>
<td>0.61 ± 0.8</td>
<td>0.60 ± 0.88</td>
<td>1.520</td>
<td>0.14</td>
<td>0.59 ± 0.95</td>
<td>1.69</td>
<td>0.10</td>
<td>0.59 ± 0.95</td>
<td>2.77</td>
<td>0.01</td>
<td>0.60 ± 0.89</td>
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<td>0.03</td>
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<td>Diabeti c</td>
<td>T. bilirubin</td>
<td>0.80 ± 0.84</td>
<td>0.78 ± 0.73</td>
<td>2.785</td>
<td>0.00</td>
<td>0.77 ± 0.71</td>
<td>3.66</td>
<td>0.00</td>
<td>0.75 ± 0.82</td>
<td>5.67</td>
<td>0.00</td>
<td>0.74 ± 0.91</td>
<td>7.08</td>
<td>0.00</td>
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<tr>
<td></td>
<td>D. bilirubin</td>
<td>0.19 ± 0.58</td>
<td>0.19 ± 0.43</td>
<td>0.585</td>
<td>0.56</td>
<td>0.19 ± 0.41</td>
<td>0.58</td>
<td>0.56</td>
<td>0.18 ± 0.35</td>
<td>2.78</td>
<td>0.00</td>
<td>0.18 ± 0.40</td>
<td>1.80</td>
<td>0.07</td>
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<td>I. bilirubin</td>
<td>0.61 ± 0.67</td>
<td>0.59 ± 0.58</td>
<td>3.522</td>
<td>0.00</td>
<td>0.58 ± 0.61</td>
<td>3.60</td>
<td>0.00</td>
<td>0.57 ± 0.73</td>
<td>4.30</td>
<td>0.00</td>
<td>0.56 ± 0.78</td>
<td>5.45</td>
<td>0.00</td>
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</table>

Data are expressed as Mean±S.D.  
(\(P \geq 0.05\)): insignificant  
(\(P < 0.05\)): significant  
(\(P < 0.01\)): highly significant  
(\(P < 0.001\)): very highly significant
**Fig. 6:** Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum total bilirubin level (mg/dl) in normal control subjects and diabetic patients after 1,2,3 & 6 months of treatment.

**Fig. 7:** Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum direct bilirubin level (mg/dl) in normal control subjects and diabetic patients after 1,2,3 & 6 months of treatment.

**Fig. 8:** Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum indirect bilirubin level (mg/dl) in normal control subjects and diabetic patients after 1,2,3 & 6 months of treatment.
Table 4: Effect of *Nigella sativa* tea daily treatment (5gm/day) on blood urea and serum creatinine levels (mg/dl) in normal control subjects and diabetic patients after 1,2,3 & 6 months of treatment.

<table>
<thead>
<tr>
<th>Time Group</th>
<th>Parameter</th>
<th>Before</th>
<th>After 1st month</th>
<th>After 2nd month</th>
<th>After 3rd month</th>
<th>After 6th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Urea</td>
<td>20.70 ± 4.91</td>
<td>20.04 ± 4.54</td>
<td>19.41 ± 4.59</td>
<td>3.84 ± 2</td>
<td>0.00</td>
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<tr>
<td></td>
<td>Creatinine</td>
<td>0.59 ± 0.16</td>
<td>0.53 ± 0.14</td>
<td>0.61 ± 0.14</td>
<td>-</td>
<td>0.75</td>
</tr>
<tr>
<td>Diabetic</td>
<td>Urea</td>
<td>34.54 ± 8.98</td>
<td>32.54 ± 6.32</td>
<td>28.10 ± 6.32</td>
<td>6.03 ± 8</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>0.77 ± 0.37</td>
<td>0.67 ± 0.32</td>
<td>0.71 ± 0.31</td>
<td>0.71 ± 0.31</td>
<td>0.75 ± 0.31</td>
</tr>
</tbody>
</table>

Data are expressed as Mean±S.D.  
(P≥0.05): insignificant  
(P<0.05): significant  
(P<0.01): highly significant  
(P<0.001): very highly significant

**Blood urea**

![Blood urea graph](image1)

Fig. 9: Effect of *Nigella sativa* tea daily treatment (5gm/day) on blood urea level (mg/dl) in normal control subjects and diabetic patients after 1,2,3 & 6 months of treatment.

**Serum creatinine**

![Serum creatinine graph](image2)

Fig. 10: Effect of *Nigella sativa* tea daily treatment (5gm/day) on serum creatinine level (mg/dl) in normal control subjects and diabetic patients after 1,2,3 & 6 months of treatment.

**Discussion:**

Diabetes is a chronic disease characterized by disordered metabolism with inappropriately high blood sugar (Sankaranarayanan and Pari, 2011). It is a multifactorial disease, associated with a number of microvascular
(retinopathy, neuropathy and nephropathy) and macrovascular (ischemic heart disease, cerebrovascular disease and peripheral vascular diseases) complications (Heydari et al., 2010). The treatment of DM includes weight loss, regular physical activity (American Diabetes Association, 2008), pharmacologic approaches (Karnib and Ziyadah, 2010) and even using the natural remedy (Bamosa et al., 2010).

*Nigella sativa*, commonly named as black seed or black cumin, is an annual herb incorporated in diets and everyday lifestyles to promote health and to treat diseases (Sankaranarayanan and Pari, 2011). Traditionally it has been in use in many Middle Eastern countries as a natural remedy for DM. A few studies showed that it can reduce blood glucose level in humans (Bamosa et al., 2010). Many studies have examined the antidiabetic effect of *N. sativa* in a plant mixture (Al-Awadi et al., 1991; Eskander et al., 1995; El-Shabrawy and Nada, 1996), powder (El-Naggar and El-Deib, 1992) or oil (Al-Hader et al., 1993) in normal and in diabetic animal models (Meddah et al., 2009). However, no one studied the effect of *N. sativa* as a tea (hot water extract).

In the present work, *N. sativa* was added as a tea to the usual OAD, diet and exercises. The effect of six months treatment with *N. sativa* tea showed a very highly significant decrease in the levels of fasting (FBG) and postprandial (PPBG) blood glucose in the normal control group. In case of diabetic group, there was a very highly significant decrease in the levels of both FBG and PPBG. The hypoglycemic effect of *N. sativa* tea reported here is in agreement with previous reports in normal control and diabetic human subjects who were treated with *N. sativa* powder (Bamosa et al., 2010). This improvement in glucose level appears to be due to the six months treatment with *N. sativa* tea.

Glycohemoglobin (HbA\textsubscript{1c}) is largely affected by DM (Meral et al., 2004). It is used clinically as an indicator for chronic control of plasma glucose levels. Since HbA\textsubscript{1c} reflects plasma glucose levels for the past 2–3 months (Koga et al., 2011). Using six months treatment with *N. sativa* tea in the present work showed a very highly significant decrease in the level of HbA\textsubscript{1c} in both normal control and diabetic groups. The decrease by *N. sativa* tea reported here is in agreement with Fararh et al. (2005) as they found that thymoquinone (TQ) the main active constituent of the seed brought about a decrease in total glycohemoglobin in diabetic hamsters. This decrease in total glycohemoglobin levels reflects the adequate and effective action of *N. sativa* in long-term reduction of diabetic hyperglycemia. Such improvement suggests the use of *N. sativa* tea as an adjuvant therapy for DM.

In type 2 diabetes mellitus, fatty liver is more closely linked to obesity than to hyperglycemia. Excessive dietary fats and carbohydrates are metabolized into free fatty acids that are subsequently stored in hepatocytes. It has been reported that fatty liver influences severity of hepatic insulin resistance (Kelley et al., 2003). Measurement of ALT and AST enzymes activity in serum is of important value because it helps to assess the state of the liver. Normally serum ALT and AST levels are low, but these enzymes are released into circulation after cellular damage and increased because they are cytoplasmic in location (Al-Kubaisy and Al-Noaemi, 2007). The treatment of alloxan-induced diabetic rats for 30 days with 1 gm/kg body weight of whole powder *N. sativa* seeds induced a significant decrease in the elevated AST and ALT levels (El-Shamy et al., 2000). TQ protected the liver enzymes (ALT and AST) leakage in isolated rat hepatocytes (Daba and Abdel–Rahman, 1998). Abuelgasim et al. (2008) reported a significant improvement in the elevated levels of AST and ALT in rats treated with methanolic extract of *N. sativa* seeds. In addition, Al-Gmadi (2003) and Ilhan and Seckin (2005) stated a marked inhibition of increased enzyme plasma level in animals treated with *N. sativa* seeds extract.

Regarding to the present results, the six months treatment with *N. sativa* tea showed a significant decrease in the level of AST and a very highly significant decrease in the level of ALT in normal control group. In the case of diabetic group, there was an insignificant decrease in the level of both AST and ALT.

In the same way, diabetes affects the serum concentration of unconjugated and of conjugated bilirubin. It was increased 1.6 and 8 fold respectively (Gonzalez and Feyer, 1992). Serum bilirubin was significantly increased in both the severe and mild alloxan-diabetic rats (Mikhail et al., 1978). In the present work, the treatment with *N. sativa* tea for six months showed a very highly significant decrease in the level of serum total and direct bilirubin and a significant decrease in the level of indirect bilirubin in normal control group. El-Dakhakhny et al. (2000) showed that the daily administration of *N. sativa* oil (800 mg/kg b.wt) for 4 weeks did not adversely affect the serum bilirubin in normal albino rats. This result seems to be in conflict with our results. In the case of diabetic group in the present work, there was a very highly significant decrease in the level of serum total and indirect bilirubin with an insignificant decrease in the level of direct bilirubin.

Results of the liver functions tests in this study may suggest that the use of *N. sativa* tea for six months may help to improve the state of the liver by preventing cellular damage and so inhibits enzymes to release into blood circulation. *N. sativa* was also found to have a hepatoprotective effect in diabetic patients (Farah et al., 2010).

Diabetes can also affect the kidney functions and lead to diabetic nephropathy. Incipient nephropathy usually occurs after 6–15 years of DM (Fraser and Phillips, 2007). However, most people with diabetes do not develop severe enough renal dysfunction to progress to kidney failure (Karnib and Ziyadah, 2010). Plasma creatinine concentration is a more potent indicator than the urea concentration in the first phases of kidney
disease. Furthermore, urea concentration begins to increase only after parenchyma tissue injury (Yaman and Balikci, 2010).

The treatment with *N. sativa* tea for six months in the present study showed a very highly significant decrease in the level of both urea and creatinine in the normal control and diabetic groups after six months of treatment. In agreement with these results, Ali (2004) and Khan and Sultan (2005) reported that the treatment with *N. sativa* oil produced a dose-dependent amelioration of increased urea and creatinine in rats. Sayed–Ahmed and Nagi (2007), suggested that TQ supplementation prevents the development of renal failure by a mechanism related, at least in part, to its ability to decrease oxidative stress and to preserve the activity of the anti-oxidant enzymes, as well as, its ability to prevent the energy decline in kidney tissue.

In conclusion, the six months treatment with *N. sativa* tea added to the usual OAD, diet and exercises showed improvement in glucose level, glycoheamoglobin, AST, ALT, serum total, direct and indirect bilirubin, serum creatinine and blood urea. This improvement suggests the use of *N. sativa* tea in diabetic patients as an adjuvant therapy for DM.

Acknowledgment

Thanks to Dr. Manal Abdel-hamid Ali Elbaiomy, Lecturer of Internal Medicine, Ain Shams Specialized Hospital for her help in selecting some of the patients of this work.

References


