The analysis of the protective feature of *Nigella sativa* in reducing Carbimazole toxicity including liver and kidney parameters on Albino male rats

Shatha Hussein Kadhim¹, Amal Umran Musa¹, Zahraa Abed al-kareem¹, Moayad Mijbil Ubaid², Noor D. Aziz¹

¹College of Pharmacy, University of Kerbala, Kerbala, Iraq.  
²College of Basic Education, University of Summer, Thi-Qar, Iraq.

**ARTICLE INFORMATION**

**Article History:**
Submitted: 21 December 2017  
Revised version received: 30 December 2017  
Accepted: 2 January 2018  
Published online: 1 March 2018

**KEY WORDS:**
*Nigella sativa*  
Carbimazole  
Renal toxicity  
Hyperthyroidism

**Corresponding author:**
Moayad Mijbil Ubaid  
Email: moayadmijbil@gmail.com  
College of Basic Education  
University of Summer  
Thi-Qar  
Iraq.

**ABSTRACT**

**Objective:** Carbimazole is widespread drug utilized for treating hyperthyroidism but, carbimazole usage was associated with adverse on some organs. Also, carbimazole overdose has been linked to nephritis in rats, while, *Nigella sativa* a medical plant has many antioxidant effects against liver and kidney toxicity so, the aim of study was to explore the protective effect of *Nigella sativa* against carbimazole-induced hepatic and renal toxicity in rats.

**Methods:** The experiment was done on 24 male albino rats in Karbala University /animal house of Pharmacy College for two months period, this work considered the agreement of the animal rights in the college. The rats were divided into four groups, the first group is control which represented healthy animals, the second group is carbimazole group was drenched orally with 1.6 mg/kg/day of carbimazole, the third group was drenched orally with 4ml/kg of *Nigella* for three days in a week plus 1.6 mg/kg/day of carbimazole and last group was drenched 4ml/kg of *Nigella* for three days per week. The samples of Blood were collected for lab analysis including the liver and kidney functions and tissues were underwent for histopathological evaluation.

**Results:** The study demonstrated significant effect of *Nigella* in reducing the toxicity of "carbimazole" in both biochemical parameters for liver and kidney ("ALT, AST, ALP, Urea, Creatinine") and in histological section as mentioned below in results.

**Conclusion:** From the results we concluded that *Nigella sativa* may have protective effect against "carbimazole toxicity".

**INTRODUCTION**

Hyperthyroidism was considered as sub-clinical case when there were slightly elevation in peripheral thyroid hormones, but still with normal range. Hypothalamus-pituitary axis sensitive to elevation of thyroid hormones and ultimately a reverse feedback mechanism will outcome trough decreasing thyrothrophic hormone (TSH), indeed subclinical hyperthyroidism may be symptomatic or asymptomatic. In the United States they found hyperthyroidism prevalence is about 1.2% including 0.7% subclinical conditions and 0.5% explicit
cases. The ultimate current causes include Graves’ disease, toxic variant of multinodular thyroid disease and toxic adenoma. Carbimazole is widespread drug utilized for treating hyperthyroidism, it is 3-carboxethoxy methimazole derivative. After treatment using this drug for 2.4 and 6 weeks durations there was significant reduction in thyroid-stimulating hormone and thyrotropin-binding inhibitory immunoglobulins. Furthermore, usage of carbimazole was associated with adverse effect on certain organs. Ali et al. announced that carbimazole resulted in necrosis of renal tubules of rats. Marzuela et al. pointed that carbimazole was ambidextrous in producing cholestatic hepatitis and acute pancreatitis, necrotizing glomerulonephritis and pulmonary hemorrhage all were related to carbimazole usage. Heidari et al. pointed that carbimazole usage caused a granulocytosis and severe cholestatic jaundice with hepatotoxicity. It induce intracanalicular cholestatic jaundice and little mononuclear cell infiltrate within the portal triades through blastogenic response of patient lymphocytes involving antigen stimulating immune reaction particularly cholestasis created by sensitized lymphocytes.

Carbimazole toxicity is associated with kidney impairment shown as different glomerular defects such as necrotizing glomerulonephritis, lupus nephritis or vasculitis. The flowering plant Nigella sativa belongs to Ranunculaceae family which is annual herbaceous plant is currently called black seed or black cumin. Nigella sativa has been vastly used in Middle east, Far East, South east Asia, Europe and India as spicy flavors and inbred therapy for many sicknesses as infections, asthma, vertigo, headache, obesity, hypertension, cough influenza, vertigo and fever. It was stated that Nigella sativa presents plentiful pharmacological consequences like antioxidants, anti-inflammatory, antimicrobial, anti diabetic, anti hypertensive, Neuroprotective and anticarcinogenic. The properties of Nigella sativa of main chemical components are alkaloid, 2 % essential oil, 37% fixed oil, proteins, vitamins, carbohydrates and minerals. The aims of the study: The aim of the present study is to evaluate the "protective effect" of Nigella sativa in the toxicity of carbimazole in albino rats. MATERIALS AND METHODS Animals and chemicals Twenty four male albino rats, weighting 300-350 g were used in this study the animals were housed in animal house of University of Kerbala/College of Pharmacy with suitable location (suitable temperature and 12:12 dark:light), where given free access to food and water. These animals were divided into four groups. 1-Control group: was nourished with basic food for two months. 2-Carbimazole group: was drenched 1.6 mg/kg/day of carbimazole, for two months. 3-(Nigella + carbimazole) group: was drenched 1.6 mg/kg/day of carbimazole +4 /ml/kg/three days in a week of Nigella for two months. 4-Nigella sativa group: was drenched 4 ml/kg/ three days in week of nigel, for two months. Biochemical measurements For biochemical study "Aspartate aminotransferase and Alanine aminotransferase" were colorimetrically identified in regard to early research as well as alkaline phosphatase, creatinine and urea were examined. Histopathological preparations The treated animals were sacrificed after two months by cervical decapitation, rats were dissected immediately after decapitation then the liver and kidney were removed and fixed with 10% formalin. After this step they were soaked in an ascending series of alcohol for dehydration, then clearance was done by xylene double changes and firm in molted paraffin wax, microtome (HM 355S Automatic Microtome) was used to slice wax in little thickness of five microns followed by mounting on proper slides. then staining with Ehrlichs heamatoxylin and counterstained with eosin, at last the pathologist examined the slides in Olympus microscope at (400x). Statistical analysis Data were expressed as mean ± SE. Differences between control and other experimental groups were tested for statistical significance using SPSS version 20 one-way analysis of variances (ANOVA) (post hoc and LSD). RESULTS Biochemical results Table 1 Show the effect of Nigella sativa against carbimazole toxicity on liver and kidney function of male rats, there were significant reducing in ALT, AST, ALP, Urea, Creatinine values 49.66, 77.50, 119.66, 46.83, 0.21 ; respectivily, as compared with carbimazole group 84.33, 104.16, 152, 67, 0.37 , while in Nigella group the results were near to control group 44.33, 75.66, 108.50, 42.66, 0.24. Table1: The effect of Nigella sativa against carbimazole toxicity on liver and kidney function of male rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ALT U/L</th>
<th>AST U/L</th>
<th>ALP U/L</th>
<th>Urea Mg/dl</th>
<th>Creatinine Mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>41.83±2.38</td>
<td>67.50±0.92</td>
<td>100.33±0.76</td>
<td>38.33±0.80</td>
<td>0.23±0.009</td>
</tr>
<tr>
<td>Carbimazole</td>
<td>84.33±2.66</td>
<td>104.16±2.35</td>
<td>152.00±2.90</td>
<td>67.00±2.0</td>
<td>0.37±0.006</td>
</tr>
<tr>
<td>Nigella + carbimazole</td>
<td>49.66±1.49</td>
<td>77.50±2.60</td>
<td>119.66±0.55</td>
<td>46.83±1.4</td>
<td>0.21±0.008</td>
</tr>
<tr>
<td>Nigella sativa</td>
<td>42.33±1.58</td>
<td>69.66±1.40</td>
<td>103.50±1.52</td>
<td>40.66±1.8</td>
<td>0.22±0.003</td>
</tr>
</tbody>
</table>

Different small letter means significant change among groups. P ≤ 0.05. Histological results 1- Control group : In case of liver section in this group was noticed normal central vein with hepatocytes arranged radially around it. While in kidney the section showed normal glomeruli and tubules. 2- Carbimazole group: The liver section showed significant congestion, focal degeneration and single...
cell coagulated necrosis, while in kidney there was well defined tubular epithelial cell necrosis, glomerular congestion, with focal mild chronic inflammatory cellular aggregates. (tubules affected rather than glomeruli).

3- Carbimazole + Nigella group: In case of liver: regular hepatocytic plates and lobular architecture with still seen are the necrosis and little degeneration. While in kidney section: partial response to treatment by decrease congestion, absence of inflammation although still necrosis seen.

4- Nigella group: in liver section: No remarkable pathology seen in liver tissue, in the case of kidney: preserved tubular and glomerular architecture with intraluminal proteinous secretion, no necrosis or degeneration.
DISCUSSION

Carbimazole overdose causes negative impacts on liver and renal tissues through enzyme activities of rats, so from the following results there were significant elevation in (ALT, AST, ALP) values, this may be as a result of hepatocellular damage by the toxicity of carbimazole which led to diffuse these enzymes from damaged liver cells to blood stream, this opinion agreed with 54,55. Also, Ajayi and Akhigbe reported an increment in aminotransferases following achieving hypothyroidism by carbimazole treating rats 56. They appended that lytic process in hepatocytes was resulted from carbimazole usage. Moreover Kota et al 57 reported that "carbimazole induced cholestatic hepatitis in Graves disease", so this results gave an evidence for hepatorenal toxicity of rats by carbimazole. The elevation in creatinin level might be accounted to the disorder of kidney function and considered as a good indicator of renal toxicity of carbimazole. The path histological results for hepatorenal exhibits the damage of hepatocytes cells as necrosis and degeneration, inflammation ,furthermore losing spacing , likewise necrosis in glomeruli and damage in renal tubules that is agreed with previous studies 54,55.

On the other hand Nigella sativa showed "protective effect" in reducing and preventing the damage which induced by carbimazole, so from the table there are significant effect of Nigella in shifting hepatorenal parameters ALT, AST, ALP and creatinin urea to normal value, that is clear argument of the protective impacts of this antioxidant item in repairing the damaged cells that is agreed with Salama et al and El Daly 55,56, who depicted that the administration of Nigella sativa concomitant with alternative drenched carbimazole decreased the rise of serum creatinin and urea concentrations, this is a good evidence on Nigella sativa as anti-inflammatory which was return to its inhibit effects on cyclooxygenase and lipoxygenase enzymes in line with Salem ML 57. Moreover studies showed that Nigella has protective effect in removing the toxin from cells or reducing its amount by repairing liver and kidney tissues and reducing degeneration and inflammation in cells and vessels . From these results we conclude the protective effect of Nigella sativa against carbimazole toxicity.

Conclusions

From our results we conclude that Nigella sativa may have anti-inflammatory and protective effect against Carbimazole toxicity.

Recommendation

We recommended deeply studies on the effect of Nigella sativa on antioxidant parameters.

REFERENCES


