Curative and hepatoprotective action of fenugreek (Trigonellafoenumgraecum) seeds against cisplatin induced oxidative liver damage in male albino rats

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Abstract

Fenugreek is one of several herbal medicines whose seeds and leaves are used either as food or as drink. The present study was designed to investigate possible potential hepatocurative & hepatoprotective activity of 5% and 10% of fenugreek (Trigonellafoenumgraecum) seeds against cisplatin (5mg/kg body wt.) induced oxidative liver damage in male albino rats. The experimental protocol designed as the animals (42 rats) were divided into seven groups including both curative and protective groups (six rats each): Group (1) Negative control group was fed on basal diet only for 28 days and curative groups including subgroups (2,3,4) were injected interaperitoneal by cisplatin (5mg/kg body wt.) from the first day and waiting for 24 hours to induce hepatotoxicity as follows: curative Positive control group (subgroup 2) was fed on basal diet after injection, subgroup (3,4) was fed basal diet +5% and 10% fenugreek seeds powder respectively after injection by cisplatin. While Protective groups including subgroups (5,6,7), they were injected with cisplatin interaperitoneal on the last day of the experiment and kept 24 hours after injection and divided as follows: protective Positive control group (subgroup 5) was fed basal diet after injection, subgroup (3,4) was fed basal diet +5% and 10% fenugreek seeds powder respectively after injection by cisplatin. Besides, nutritional and biological parameters were recorded (FI, BWG%, FER). The results showed that fenugreek seeds powder at 5% and 10% intake in curative and protective groups improved feed intake, the liver function, and antioxidant enzymes compared with positive control groups (injected with cisplatin). It can be concluded that fenugreek seed improved the activities of liver functions and antioxidant enzymes against cisplatin that induced oxidative liver injury.

Key words: fenugreek seeds, cisplatin (CIS), oxidative liver injury, male albino rats

Introduction

Fenugreek (Trigonella toenum graecum Linn) is an annual herb that belongs to the family Leguminosae. The seeds of fenugreek are commonly used in the Middle East and South Asia as a spice in food preparation and used as traditional medicines in diabetes, highcholesterol, inflammations (AL-Mashhadani, 2017). Fenugreek, like other legumes, is a good source of dietary protein (about 24%), fatty acids (5-10%) which include linoleic, linolenic, oleic and palmatic. It has 45-65% total carbohydrates with 15% of galactomannose (soluble fiber) and other active compounds required in a human body such as saponins, coumarin and fenugreekine (Eidi et al., 2007).
Wesam M. Abd-Elrahman

Fenugreek was found to treat glucose and lipid homeostasis in several metabolic disorders (Raju and Bird, 2006). The seeds have been shown to possess hypoglycemic action (Srinivasan, 2005 and Gad, et al., 2006). Furthermore, fenugreek seed extract was found to decrease plasma triglycerides (Handa, 2005) and to reduce triglycerides accumulation in the liver (Raju and Bird, 2006). It was reported, also, that fenugreek seed polyphenols had a positive influence on both lipid profile and on quantitative and qualitative properties of collagen in hepatotoxicity (Kaviarasan, et al., 2007 and Dixit, et al., 2005). Furthermore, fenugreek was shown to possess antioxidant activity, and to afford protection against cancer of the breast (Amin, et al., 2005) and colon (Raju, et al., 2004).

The liver plays a major role in transforming and clearing chemicals which lead to increase its susceptibility to the toxicity from these agents (Abu-Raghif, et al., 2016). Liver diseases are one of the major causes of mortality and morbidity worldwide (Abboud and Kaplowitz, 2007). Drugs are an important cause of liver injury, more than 900 drugs, toxins, and herbs have been reported to cause hepatic injury. Cisplatin [cis-diamminechloroplatinum (II)] is a potent antineoplastic agent used for the treatment of a wide range of cancers (Abu-Raghif, et al., 2016). Nevertheless, this drug has severe toxic effects that interfere with its therapeutic efficacy, namely nephrotoxicity and hepatotoxicity. Although the nephrotoxicity of cisplatin has been recognized as the most important dose-limiting factor, little is known about cisplatin induced liver injury. Hepatotoxicity is not considered as a dose limiting toxicity for cisplatin, but liver toxicity can occur when the antineoplastic drug is administered at high doses (Ziccaet al., 2002). Oxidative stress is one of the most important mechanisms involved in cisplatin induced toxicity. The mitochondrion is the primary target for cisplatin induced oxidative stress, resulting in loss of mitochondrial protein-SH, inhibition of calcium uptake and a reduction in the mitochondrial membrane potential (Saadet al, 2004).

This study has been carried out to evaluate possible advantage that could be obtained by using fenugreek seed powder as curative or protective effect against cisplatin-induced liver damage in male albino rats.

**Material and methods**

**Materials:**
1) Fenugreek seeds (*Trigonellafoenumgaraecum*) were purchased from Field Crops Research Institute, Agricultural Research Center, Giza- Egypt.
2) Casein, vitamins, minerals, cellulose and choline chloride were obtained from Morgan Company for chemical laboratory, Cairo, Egypt.
3) Normal male albino rats (Sprague Dawley Strain) weighing (150±10g) were obtained from vaccine and immunity organization Helwan Farm, Cairo, Egypt.
4) Cisplatin was obtained from the Cairo Company for Chemical Trading, Cairo, Egypt.

**Methods:**
Preparation of fenugreek seeds:
Fenugreek seeds were washed dried and crushed using electric blender to a fine powder which was packed in air-tight plastic bags till use for basal diet supplementation.

Chemical composition of fenugreek:
Chemical composition of fenugreek (moisture, ash, crude protein, and fat) were determined according to the methods of the *AOAC (2010).* While total carbohydrates were estimated by difference from initial weight of the sample as follows: - Carbohydrates% = 100% - (%moisture + % protein + % fat +%ash).
Phenolic compounds of fenugreek

The polyphenol compounds in fenugreek seeds powder was fractionated and identified for phenolic compounds and flavonoids compounds by HPLC, according to the method described by Tarola et al., (2013).

Experimental design:

A total of 42 rats were housed in well-aerated cages under hygienic condition and fed on basal diet for one week for adaptation. After this week, rats were divided into seven groups including both curative and protective groups (six rats each).

- **Group (1)** was kept as negative control group and was fed on basal diet only according to Reeves et al., (1993) during the whole period of the experiment (28 days).

The other thirty-six rats were divided into two main groups (18 rats for each main group). The **Secand main group** (18 rats) were injected interaperitoneal with Cisplatin (5mg/kg body wt.) once only in the first day of the experimental period and kept as curative groups according to Yogesh et al., (2010), then on the next day it was divided into three subgroups as follows:

- **subgroup (2)** was considered as control positive (curative) and was fed on basal diet
- **subgroup (3)** was fed on basal diet + 5% fenugreek seeds powder replacing equivalent amount from the basal diet
- **subgroup (4)** was fed on basal diet + 10% fenugreek seeds powder replacing equivalent amount from the basal diet

The **Third main group** (18 rats) were divided into three subgroups as follows:

- **subgroup (5)** was considered as control positive (protective) and it was fed on basal diet
- **subgroup (6)** was fed on basal diet + 5% fenugreek seeds powder replacing equivalent amount from the basal diet
- **subgroup (7)** was fed on basal diet + 10% fenugreek seeds powder replacing equivalent amount from the basal diet

Subgroups (5, 6, 7) were injected interaperitoneal with cisplatin (5mg/kg body wt.) and kept for 24 hours after injection.

Feed intake (FI), body weight gain (BWG) and feed efficiency ratio (FER) were determined according to Chapman et al. (1959). At the end of experimental period, all rats were fasted overnight (12 hours), sacrificed and the blood samples were collected and centrifuged to obtain the serum which was kept frozen till analysis. Livers were collected after being removal, cleaned in saline solution, dried by filter paper and weighted, and rapidly taken on ice bags and frozen at –18°C, until used for assessment of lipid peroxidation and antioxidant activity in liver tissue.

**Biochemical analysis of serum:**

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined according to Bergmeyer et al., (1986), albumin according to Drupt, (1974), total protein according to Sonnenwirth and Jaret (1980). Globulin and albumin/ globulin (A/G) were calculated according to Busher, (1990) using the following equation:

\[ \text{Globulin} = \text{total protein} - \text{albumin} \]

**Assessment of Oxidant/Antioxidant Activity in liver:**

After defrosting livers were homogenized and centrifuged at 10,000 rpm at 0°C for 20 min. the supernatant part was used for estimation of different antioxidant level by calorimetric method using spectrophotometer (Merck thermo spectronic, Model NO. UV-1, double beam), Lipid peroxidation by thiobarbuturic acid-reactive substances (TBARS) methods (Uchiyama and Mihara 1978), Superoxide dismutase (SOD) by...
the method developed by Misra and Fridovich, (1972) and Catalase (CAT) by colorimetric assay (Sinha,1972).

Statistical analysis:
Results are expressed as mean ± SD. Data were statistically analyzed using one-way analysis of variance “ANOVA” according to Armitage& Berry, (1987). Computer software system SPSS (version 15).

Result and discussion

Chemical composition of fenugreek seeds
Fenugreek was analyzed for chemical composition (moisture, protein, carbohydrates, fat, crude fiber and ash). The obtained results showed in table (1) on the dry weight basis. The results showed that the crude protein, total carbohydrates, fat content, crude fiber and ash were 27.16, 46.3, 3.12, 10.82 and 4.20% on dry weight, respectively. The present results are in agreement with Mehrfarinet al., (2010) who concluded that fenugreek seed contains 45-60% carbohydrates, mainly mucilaginous fiber (galactomannans), 20-30% proteins, 5 - 10% fixed oils (lipids). Also our data are in agreement with Meghwal and Goswami, (2012) and Mullaicharamet al., (2013) and Khorshidianet al., (2016). On the other hand our results disagreed with El-Bairi et al., (2017) who reported that fenugreek contains 23–26% protein, 6–7% fat and 58% carbohydrates of which about 25% is dietary fiber.

Table (1)

<table>
<thead>
<tr>
<th>Compositions</th>
<th>gm/ 100gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture</td>
<td>8.4</td>
</tr>
<tr>
<td>Protein</td>
<td>27.16</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>46.3</td>
</tr>
<tr>
<td>Fat</td>
<td>3.12</td>
</tr>
<tr>
<td>Crude Fiber</td>
<td>10.82</td>
</tr>
<tr>
<td>Ash</td>
<td>4.20</td>
</tr>
</tbody>
</table>

Phenolic compounds of fenugreek seeds
Fenugreek seeds analyzed for their phenolic compounds are shown in table (2). The present results are in agreement with Akbari et al., (2012) who showed that, numbers of important phenolic and styrylic acid derivatives, such as p-coumaric acid, caffeic acid, chlorogenic acid, coumarin derivatives, namely hymecromone, trigoforin, trigocoumarin, scopoletin, and cyclooctane derivatives, such as schizandrin, were isolated from different parts of fenugreek plant.
Nutritional parameters of the biological experiment:

Food intake, body weight gain, and feed efficiency ratio were determined and the results are tabulated in Table (3).

- It could be observed that there are no significant difference between (-ve) control and the curative groups in food intake (FI) while there are significant increase between (-ve) control and protective groups except (subgroup 7).
- Results of final body weight showed significant decrease in curative subgroups (2, 3, 4) when compared to normal rats (group 1) (17.11±1.21a, 17.08±.43a and 17.33±.72a respectively) while Protective subgroups (6, 7) showed significant increase (P<0.05) compared with normal rats (group 1).
- The results in the table 3 showed significant decrease in feed efficiency ratio was observed at positive controls (subgroups 2 and 5) groups compared to negative group (1.10 ± 1.0a and 1.16 ± 0.8 a, 1.35 ± 1.7 b respectively). The best results were protective fenugreek subgroups (6 and 7).
Table (3)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>FI (g/day)</th>
<th>BWG (g)</th>
<th>(FER)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>I</td>
<td>Group (1) (-ve) Control</td>
<td>14.48 ± .80 a</td>
<td>19.46 ±1.75 b</td>
<td>1.35 ±17 b</td>
</tr>
<tr>
<td>II</td>
<td>Curative groups</td>
<td>subgroup (2)</td>
<td>15.86 ±.54 ab</td>
<td>17.11 ±1.21 a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>subgroup (3)</td>
<td>15.96 ±.48 ab</td>
<td>17.08 ±4.3 a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>subgroup (4)</td>
<td>14.86 ±.54 a</td>
<td>17.33 ±7.2 a</td>
</tr>
<tr>
<td>III</td>
<td>Protective groups</td>
<td>subgroup (5)</td>
<td>16.95 ±.47 b</td>
<td>19.80 ±1.02 b</td>
</tr>
<tr>
<td></td>
<td></td>
<td>subgroup (6)</td>
<td>17.23 ±.32 b</td>
<td>22.53 ±5.9 a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>subgroup (7)</td>
<td>15.83 ±.42 ab</td>
<td>24.81 ±1.55 b</td>
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</tbody>
</table>

Values denote arithmetic means ± SD of the mean. Means with different letters (a, b, c, d, e, f) in the same column differ significantly at (p ≥ 0.05) while those with similar letters are non-significant.


**konopelnyuket al., (2015)** illustrated two possible mechanisms of fenugreek decreasing the total body weight. Fenugreek flushes out the carbohydrates from the body before they enter the blood stream resulting in weight loss. Fenugreek seeds contain a high proportion of soluble fiber. This fiber forms a gelatinous structure which may have effects on slowing the digestion and absorption of food from the intestine and creates a sense of fullness in the abdomen, thus suppresses appetite and promotes weight loss.

**Effect of fenugreek seeds on liver functions in the curative and protective groups**

Liver enzymes of different experimental groups are reported in Table (4). Exposing rats to cisplatin showed significant (P<0.05) increase in the level of liver enzymes (AST, ALT and ALP) in curative and protective (+ve control groups) (subgroups 2 and 5). While feeding rats on fenugreek 5% significantly decreased the levels of liver enzymes in both treated and protective groups.
Table (4)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>AST (IU/L)</th>
<th>ALT (IU/L)</th>
<th>ALP (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Group (1) (-ve) Control</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>subgroup (2)</td>
<td>43.66±4.32&lt;sup&gt;a&lt;/sup&gt;</td>
<td>27.00±2.00&lt;sup&gt;a&lt;/sup&gt;</td>
<td>138.16±4.79&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>subgroup (3)</td>
<td>142.00±3.74&lt;sup&gt;f&lt;/sup&gt;</td>
<td>47.66±3.72&lt;sup&gt;c&lt;/sup&gt;</td>
<td>185.50±4.46&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>subgroup (4)</td>
<td>86.16±4.49&lt;sup&gt;c&lt;/sup&gt;</td>
<td>38.16±2.22&lt;sup&gt;b&lt;/sup&gt;</td>
<td>172.66±4.08&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>II</td>
<td>Curative groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>subgroup (5)</td>
<td>55.33±4.54&lt;sup&gt;g&lt;/sup&gt;</td>
<td>155.66±4.50&lt;sup&gt;e&lt;/sup&gt;</td>
<td>148.66±5.35&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>subgroup (6)</td>
<td>134.00±3.52&lt;sup&gt;g&lt;/sup&gt;</td>
<td>114.83±4.30&lt;sup&gt;d&lt;/sup&gt;</td>
<td>144.33±5.12&lt;sup&gt;ad&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>subgroup (7)</td>
<td>125.16±4.70&lt;sup&gt;c&lt;/sup&gt;</td>
<td>29.83±3.81&lt;sup&gt;a&lt;/sup&gt;</td>
<td>139.33±4.08&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
<tr>
<td>III</td>
<td>Protective groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>subgroup (5)</td>
<td></td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>subgroup (7)</td>
<td></td>
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</tbody>
</table>

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Cisplatin-induced nephrotoxicity through multiple mechanisms, including hypoxia, the generation of free radicals, inflammation, and apoptosis with an increase in the pro-apoptotic protein Bax and a decrease in the anti-apoptotic protein Bcl-2 (Tsuruya et al., 2003). While the mechanisms of cisplatin-induced hepatotoxicity are not fully understood (Hong et al., 2005), the link between oxidative stress and cisplatin toxicity was suggested in many experimental models (Bentli et al., 2013 & Lu and Cederbaum, 2006).

Our results showed that feeding fenugreek can prevent cisplatin induced toxicity in the liver by significantly reduction of AST, ALT, ALP, these results are in agreement with (Meera et al., 2009)and (AL-Mashhadani, 2017), they achieved that the normalization of the above enzyme levels in rat liver with the plant drugs establishes the hepato protective effect of T. foenum-graecum which may be able to induce accelerated regeneration of liver cells reducing the leakage of these enzymes into the blood. The results indicated that fenugreek significantly prevented the increased liver function marker enzyme activity induced by cisplatin, indicating an improvement of the functional status of the liver by the fenugreek.

Effect of fenugreek seeds on serum protein, albumin, globulin and albumin/globulin in the curative and protective groups (table 5)

The table shows the effect of supplemented fenugreek on total protein, albumin, globulin and albumin/globulin compared with negative control groups. Cisplatin administration (5 mg/ kg) resulted in significant increase in total protein and albumin compared with the negative control groupe. Treatment with fenugreek 5% (subgroup 3) resulted in a significant reduction in serum level of total protein and albumin compare to curative positive group (subgroup 2). There were no significant difference among protective groups and normal rats group in total protein and albumin. There were no significant difference among normal rats group (group 1) compared with curative groups in globulin and A/G while positive protective group (subgroup 5) show significant decrease in globulin compare with negative group ( group 1).
Effect of fenugreek seeds on total protein, albumin, globulin in both curative and protective groups of rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>Total protein (gm/dl)</th>
<th>albumin (gm/dl)</th>
<th>Globulin (gm/dl)</th>
<th>A/G</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>I</td>
<td>Group (1) (-ve) Control</td>
<td>3.11 ±.11\textsuperscript{bc}</td>
<td>2.46 ±.18\textsuperscript{bc}</td>
<td>.65 ±.24\textsuperscript{b}</td>
<td>4.45 ±2.43\textsuperscript{b}</td>
</tr>
<tr>
<td></td>
<td>Curative groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>subgroup (2)</td>
<td>3.48 ±.07\textsuperscript{d}</td>
<td>2.73 ±.18\textsuperscript{d}</td>
<td>.75 ±.20\textsuperscript{a}</td>
<td>3.90 ±1.26\textsuperscript{a}</td>
</tr>
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<td>subgroup (3)</td>
<td>3.00 ±.26\textsuperscript{a}</td>
<td>2.36 ±.22\textsuperscript{a}</td>
<td>.66 ±.22\textsuperscript{a}</td>
<td>4.06 ±2.06\textsuperscript{a}</td>
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<tr>
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<td>subgroup (4)</td>
<td>3.53 ±.33\textsuperscript{a}</td>
<td>2.63 ±.05\textsuperscript{a}</td>
<td>.90 ±.35\textsuperscript{b}</td>
<td>3.43 ±1.96\textsuperscript{b}</td>
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</tr>
<tr>
<td></td>
<td>subgroup (5)</td>
<td>2.83 ±.36\textsuperscript{a}</td>
<td>2.31 ±.14\textsuperscript{a}</td>
<td>.35 ±.08\textsuperscript{a}</td>
<td>6.9 ±2.08\textsuperscript{a}</td>
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<td>subgroup (6)</td>
<td>3.25 ±.27\textsuperscript{a}</td>
<td>2.43 ±.31\textsuperscript{a}</td>
<td>.81 ±.03\textsuperscript{a}</td>
<td>3.3 ±1.11\textsuperscript{a}</td>
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<td></td>
<td>subgroup (7)</td>
<td>3.38 ±.14\textsuperscript{a}</td>
<td>2.36 ±.05\textsuperscript{a}</td>
<td>1.2 ±.16\textsuperscript{a}</td>
<td>1.8 ±.30\textsuperscript{a}</td>
</tr>
</tbody>
</table>

Values denote arithmetic means ± SD of the mean. Means with different letters (a, b, c, d, e, f) in the same column differ significantly at (p ≥ 0.05) while those with similar letters are non-significant.


Effect of feeding fenugreek seedson SOD, CAT and lipid peroxide MDA in the curative and protective groups of rats (table 6)

The table illustrated the activity of liver superoxide dismutase (SOD) and catalase (CAT) which were significantly increased in treatment fenugreek subgroups (3,4) when compared with subgroup (2) (+ve control). While protective groups showed significant increase in protective fenugreek subgroups (6,7) when compared with subgroup (5). Table (6) also showed a significant decrease in liver malondialdehyde (MDA) in both positive subgroups (2 and 5) when compared with normal rat (group 1). Other treated and protective groups showed significant decrease compared with the positive groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>parameters</th>
<th>MDA Nmol/mg</th>
<th>SOD Ng/mg</th>
<th>CAT U/I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± S.D</td>
<td>Mean ± S.D</td>
<td>Mean ± S.D</td>
</tr>
<tr>
<td>I</td>
<td>Group (1) (-ve) Control</td>
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<td>.21 ±.04\textsuperscript{a}</td>
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</tr>
<tr>
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<td></td>
</tr>
<tr>
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<td>subgroup (2)</td>
<td>.41 ±.10\textsuperscript{b}</td>
<td>.12 ±.03\textsuperscript{b}</td>
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<td>subgroup (3)</td>
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<td>.22 ±.02\textsuperscript{b}</td>
<td>.17 ±.009\textsuperscript{b}</td>
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<td>subgroup (4)</td>
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<td>.19 ±.01\textsuperscript{a}</td>
<td>.19 ±.034\textsuperscript{a}</td>
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<td>Protective groups</td>
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</tr>
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<td>subgroup (5)</td>
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<td>.09 ±.01\textsuperscript{a}</td>
<td>.12 ±.018\textsuperscript{a}</td>
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<td>subgroup (6)</td>
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<td>.14 ±.01\textsuperscript{a}</td>
<td>.14 ±.028\textsuperscript{a}</td>
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<tr>
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<td>subgroup (7)</td>
<td>.11 ±.02\textsuperscript{a}</td>
<td>.15 ±.01\textsuperscript{a}</td>
<td>.16 ±.010\textsuperscript{a}</td>
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</tbody>
</table>

Values denote arithmetic means ± SD of the mean. Means with different letters (a, b, c, d, e, f) in the same column differ significantly at (p ≥ 0.05) while those with similar letters are non-significant.


Several reports have implicated free radicals and reactive oxygen species (ROS) in cisplatin toxicity associated with an increase in lipid peroxidation (LPO), decreased levels of protein bound sulphydryl groups and glutathione (Pratibha et al., 2006).

Cisplatin is a potent anticancer agents that cause a wide range of adverse effects and organ toxicity including hepatotoxicity, nephrotoxicity and vascular endothelial dysfunction that mediated by different mechanisms such as inflammation and oxidative stress (Siddik, 2003). Cisplatin-induced hepatotoxicity is a major problem in the cancer therapy (Wang and Stephen, 2005). It has been reported that cisplatin induced hepatotoxicity is closely associated with an increase in lipid peroxidation manifested by increased MDA (Eid et al., 2016). Inflammation plays an important role in cisplatin induced liver injury (Athira et al., 2016). Although the precise inflammatory mechanisms are unknown, marked attenuation of cisplatin induced liver damage by inhibition of tumor necrosis factor alpha (TNF-α) indicates that TNF-α has a central role of mediation cisplatin induced liver injury (Li et al., 2016).

**Conclusion**

In conclusion, the present work showed the curative and protective effects of fenugreek seeds against cisplatin-induced hepatic injury in rats at both levels of supplementation of fenugreek (5%, 10%).

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التأثير العلاجي والوقائي لبذور الحلبة على تلف الكبد التأكسدي الناجم عن السيزبلاتين
في ذكور الجرذان

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الحلبة من النباتات العشبية الطبية الشائع استخدام أوراقها وبذورها كطعام أوكشراب وقد أجريت هذه الدراسة لمعرفة تأثير مسحوق بذور الحلبة على تلف الكبد التأكسدى الناجم عن السيزبلاتين في ذكور الجرذان الألبينو. تم تصميم التجربة البيولوجية باستخدام ثمانية جرذان تم تقسيم كل منها إلى ثمانية مجموعات تشتمل على مجموعة ضابط سالبة ومجموعات علاجية ووقائية (ست جرذان لكل مجموعه) مكونة من مجموعه علاجية (18 جرذ) حيث تم الحقن البكيني بالسيزبلاتين (5ملليجرام/كجم من وزن جسم الجرذ) في أول يوم من بدء التجربة والانتظار لمدة 24 ساعة. و مجموعة علاجية وقائية (18 جرذ) حيث تم الحقن البكيني بالسيزبلاتين في آخر يوم من بدء التجربة بجرعة (5ملليجرام/كجم من وزن جسم الجرذ) والانتظار لمدة 24 ساعة.

المجموعة العلاجية عبارة عن ثلاث مجموعات علاجية وهي: المجموعة الفرعية (2) مجموعه ضابط موجبة علاجية حيث تغذت على الغذاء الأساسي + الحقن بالسيزبلاتين (5ملليجرام/كجم من وزن جسم الجرذ) من اليوم الأول لأحداث التسمم الكبدى. المجموعات الفرعية (3) تم تغييرنهم على غذاة أساسي مع الحقن بالسيزبلاتين بداية التجربة مع إضافة 5% و 10% من بذور الحلبة للغذاء الأساسي على التوالي.

المجموعات الوقائية تشتمل أيضاً على ثلاث مجموعات علاجية وهي كالتالي: المجموعة الفرعية (5) مجموعه ضابط وقائية موجبة تغذت على الغذاء الأساسي + الحقن بالسيزبلاتين (5ملليجرام/كجم من وزن جسم الجرذ) في نهاية مدة التجربة. المجموعات الفرعية (6) تم تغييرنهم على الغذاء الأساسي + التدعيم بنسبة 5% و 10% من بذور الحلبة على التوالي + الحقن بالسيزبلاتين في نهاية التجربة.

في نهاية التحقيبة البيولوجية تم تصوير الجرذان طوال الليل (12 ساعه) ودبيحا وأخذ عينات الدم من الأورطى لعمل التحاليل الكيميائية بالإضافة إلى أنه تم تسجيل التقديرات البيولوجية. وقد أظهرت النتائج أن مسحوق بذور الحلبة بنسبة 5% و 10% في المجموعات العلاجية والوقائية أدى إلى نقص النهار المتبقي، زيادة وزن الجسم، نسبة كفاءة الغذاء، ضمن في وظائف الكبد، والإنزيمات المضادة للأكسدة مقارنة مع المجموعات الضابطة الموجبة التي تم حقنها بالسيزبلاتين. وخلصت النتائج أن اضافة بذور الحلبة في النظام الغذائي للجرذان الألبينو بنسبة 5% و 10% قد حصدت من وظائف الكبد، وكذلك تحسنت نسبة الانزيمات المضادة للأكسدة في أنسجة الكبد ضد السيزبلاتين وانخفضت عوامل الإجهاد والالتهاب.

الكلمات المفتاحية: بذور الحلبة، تسمم الكبد، السيزبلاتين، وظائف الكبد