Effect of Dried Apricot against Carbon Tetrachloride
CCl\textsubscript{4}-Induced Hepatotoxicity in Male Rats

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Abstract: The present study was carried out to investigate the effect of feeding diets supplemented with dried apricot at three levels (5, 10 and 15%) to hepatotoxic rats after 8 weeks of treatment on body weight gain, feed efficiency ratio and relative weight of liver, serum levels of total cholesterol (TC), triglycerides (TG), lipoprotein fractions, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP); total protein (TP) and total bilirubin (TBil) were determined. Histopathological examination of liver was also performed. Forty adult male Wistar rats were divided into five groups as follows: group 1: negative control group, group 2: positive control (CCl\textsubscript{4}) group, groups 3, 4 and 5 intoxicated with CCl\textsubscript{4} and fed apricot at levels of 5, 10 and 15%, respectively. Results showed that feeding diets supplemented with dried apricot at levels of 10 and 15% to hepatotoxic rats for 8 weeks significantly improved TC, TG, lipid profile fractions, decreased the elevated serum values of liver enzymes (AST, ALT and ALP), total bilirubin and increased serum total protein in a dose depended manner when compared to the control positive group. Histopathological examination of liver sections of rats fed on diets supplemented with dried apricot showed alleviation of histological degeneration changes caused by CCl\textsubscript{4}. It can be suggest that diets supplemented with dried apricot induce potent hepatoprotective and antioxidant effects in hepatoxic rats. This study recommends that, intake of dried apricot may be beneficial for patients who suffer from liver diseases.

Key words: CCl\textsubscript{4} • Dried apricot • Liver toxicity • Liver enzymes • Rats

INTRODUCTION

Liver is the largest internal organ in human body; it has a central role in carbohydrate, protein and fat metabolism [1]. It regulates the synthesis and secretion of bile. Additionally, liver allows the detoxification of various xenobiotic [2]. Toxic injury occurs in the liver more often than other organs, because all ingested substances that are absorbed, first presented to the liver and then the liver is responsible for the metabolism and elimination of many substances [3].

Many xenobiotics such as acetaminophen, carbon tetrachloride (CCl\textsubscript{4}) and yellow phosphorus produce liver damage in a predictable and dose-dependent manner [3]. Carbon tetrachloride (CCl\textsubscript{4}) has long been known as a model toxicant in animal models for induction of acute and chronic injury, which has been applied in vitro and in vivo toxicological studies [4].

Carbon tetrachloride (CCl\textsubscript{4}) is able of causing lipid peroxidation and decreases activity of antioxidant enzymes [5]. It has been found that metabolism of carbon tetrachloride (CCl\textsubscript{4}) involves the production of highly fatal trichloromethyl radical (CCl\textsubscript{3},*) and proxy trichloromethyl (*OCCl\textsubscript{3}) free radicals through P450 bio activation [6].

Apricot (Prunus armeniaca L.) is classified under the Prunes genus of Prunoidae sub-family of the Rosacea family of the Rosales group. Apricot has an important place in human nutrition and can be used as fresh, dried or processed fruit [7]. Apricot is a good source of fiber, vitamin and minerals, in addition to high sugar content [8]. It is also thought to be a rich food in terms of antioxidants because of the carotenoids and flavonoids it contains [9]. The major phenolic compounds in apricot fruit are chlorogenic, neochlorogenic acids, (+)-catechin, (-)-epicatechin and quercetin-3-rutinoside [8]. Overall, dried...
apricots have a far greater nutritional value (e.g. especially in terms of vitamin A and minerals) than the fresh ones because all nutrients are concentrated [10].

The present study was designed to investigate the effect of feeding dried apricot at three at three levels (5, 10 and 15%) on hepatotoxic rats.

MATERIALS AND METHODS

Material

Apricot (Prunes armeniaca L): Ripe apricot used in this study was purchased from a local market, Jeddah, Kingdom of Saudi Arabia. The apricot plant was grown in Aljouf city, a north province of the Kingdom of Saudi Arabia.

Carbon Tetrachloride (CCL4): Carbon tetrachloride (CCl4) was purchased from Sigma-Aldrich Company.

Kits for Biochemical Analysis: Diagnostic commercial kits for biochemical analyses were purchased from Cayman Chemicals and BioVision Incorporated, USA.

Experimental Animals: Forty male albino rats of Wister strain weighing 200-250 grams body weight and 12 - 14 weeks old were obtained from Faculty of Pharmacy, King Abdul-Aziz University, Jeddah, Saudi Arabia.

Methods

Feeding of Rats: Diets prepared included basal diet and diet supplemented with dried apricot at three at three levels (5, 10 and 15%). The basal diet (AIN-93G) for rats was prepared according to Reeves [11]. The basal diet consists of the following: Protein (Casein) 20%; Sucrose 10%; Corn Oil 4%; Choline Chloride 0.2%; Vitamin mixture 1%; Salt mixture 3.5%; Fibers (Cellulose) 5% and the remainder is Corn Starch up to 100%. Basal diet supplemented with dried apricot at three at three levels 5, 10 and 15% means 5, 10 and 15 g dried apricot/100 g basal diet respectively. Dried apricot was estimated chemically and substituted basal diet ingredients depend on nutritional value of dried apricot (Table 1).

Table 1: Nutritional values of dried apricot per 100 g

<table>
<thead>
<tr>
<th>Carbohydrates</th>
<th>63 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugars</td>
<td>59 g</td>
</tr>
<tr>
<td>Fiber</td>
<td>7 g</td>
</tr>
<tr>
<td>Fat</td>
<td>0.5 g</td>
</tr>
<tr>
<td>Protein</td>
<td>3.4 g</td>
</tr>
</tbody>
</table>

Induction of Hepatotoxicity: Rats were treated with carbon tetrachloride (CCL4) and olive oil mixture (1:1 V/V) at the dosage of 1ml/kg b.w., i.p. for seven days to induce hepatotoxicity according to the method described by Thirumalai et al. [12].

Preparation of Dried Apricot: Fresh apricot was washed and cut into (2 × 2 × 2 cm³) cubes and packaged in polypropylene plastic containers and frozen at -20 ± 1°C for 24 h. The frozen samples were put in the freeze-dryer (ILShin BioBase) for five days until they were completely dried, then milled into powder. The lyophilized (freeze-dried) obtained apricot powder was stored at -20°C until further use. Apricot powder was chemically estimated as shown in table 1 [13].

The total weight of fresh apricot which used was 5kg; yield 600g lyophilized powder. The amount of dried apricot that used in experiment was 3360 g.

Experimental Design and Grouping of Rats: The experiment was performed on forty male mature Wistar rats distributed randomly into 5 equal groups. Rats were housed in plastic cages at a room temperature maintained at 24 ± 2°C, with fixed 12 hour lighting system.

All rats were allowed to free access to basal diet and water for one week before starting the experiment for acclimatization. After acclimatization period, the rats were allocated in to the following groups:

Group (1): Rats fed on Basal diet only; Control negative (Co –ve).

While the others four groups will be injected with carbon tetrachloride (CCL4) to induce hepatotoxicity for seven days at the beginning of the experiment. After this period blood samples were taken for measuring liver enzymes to make sure that all rats were hepatotoxic. These rats were distributed into the following groups:

Group (2): Rats fed on experimental diet only; Control positive (Con +ve).

Group (3): Rats fed on experimental diet supplemented with 5% of dried apricot.

Group (4): Rats fed on experimental diet supplemented with 10% of dried apricot.

Group (5): Rats fed on experimental diet supplemented with 15% of dried apricot.
Anesthesia and Collection of Blood Samples: Rat’s weight was recorded at the beginning of the experiment and biweekly thereafter. The percent body weight gain (BWG %) was calculated. At the end of the experimental period, the rats were fasted overnight. On the morning of the next day the rats were anesthetized by general volatile anesthesia using ether. Anesthesia was done by placing the rat in a large glass jar with a piece of cotton soaked with ether. After induction of mild anesthesia, the rat was rapidly pulled out and blood was collected. Blood samples were withdrawn by capillary microtubes (Micro Hematocrite Capillaries, Mucaps) from the retro-orbital plexuses of veins in inner canthus of the eye into plain tube with gel. The blood samples were centrifuged at 3000 rpm for 15 minutes. Serum samples were separated and frozen at -80°C until used for the biochemical analyses [14].

Serum Biochemical Analysis: Serum samples were used for determination of serum total cholesterol (TC) [15], serum triglycerides (TG) according to Trinder [16], lipoprotein fractions according to Fridewald et al. [17]. Activities of serum liver enzymes Aspartate aminotransaminase (AST), alanine aminotransferases and alkaline phosphatase (AST, ALT and ALP) were chemically estimated according to Tietz [18]. Determination of total bilirubin (TBil) according to Burtis et al. [19], total protein (TP) according to Henry [20].

Histopathological Examination: The fixed liver specimens were washed and dehydrated in ascending grades of alcohol. Specimens were then cleared in xylol, embedded in paraffin, sectioned at 4-6 microns thickness and stained with Haematoxylin and Eosin stain for histopathological examination as described by Hayat [21] and examined microscopically.

Statistical Analysis: All data obtained results were analyzed using statistical package for the social sciences (SPSS) for windows, version 20 (SPSS Inc., Chicago, IL, USA). Collected data were presented as mean± standard deviation (SD). Analysis of variance (ANOVA) test and Post hoc test were used for determining the significances among different groups according to Armitage et al. [22]. All differences were considered significant at P-values were P < 0.05.

RESULTS

Results in Table (2) showed the effect of dried apricot on initial body weight, final body weight and body weight gain percent (BWG %) in hepatotoxic rats.

Data recorded in Table 2 showed that there were no significant differences in initial body weight between all experimental groups. A significant (P< 0.05 ) decrease was observed in the final body weight of hepatotoxic rats (positive control group), compared to the normal rats (negative control group) as shown in Table 2. Feeding diet supplemented with dried apricot at levels of 5, 10 and 15%, significantly (P< 0.05) increased the final body weight when compared to the hepatotoxic rats (positive control group) as recorded in Table 2.

Concerning body weight gain percent, the results showed that there was a significant decrease in the hepatotoxic rats (positive control group) when compared to normal rats (negative control group). Feeding diet supplemented with dried apricot at levels of 5, 10 and 15% significantly (P < 0.05) increased the BWG % when compared to hepatotoxic rats (positive control group) as shown in Table 2.

Feed intake and feed efficiency ratio (FER) of hepatotoxic-rats treated with diets supplemented with dried apricot at three levels (5, 10 and 15%) are shown in Table 3.

Feed intake was significantly (P< 0.05) decreased in the hepatotoxic rats (positive control group), compared to normal rats (negative control group). Feeding diets supplemented with dried apricot at three levels 5, 10 and 15% significantly (P< 0.05) increased feed intake as compared to hepatotoxic rats (positive control group). It is clear from Table 3 that FER in hepatotoxic rats (positive control group) significantly (P< 0.05) decreased when compared to normal rats (negative control group). Significant (P< 0.05) increases were observed in rats fed on diets supplemented with dried apricot at three levels 5, 10 and 15%, as compared to the positive control group.

Data in Table 4 demonstrated that the rats acutely intoxicated by CCL₄ had significant (P < 0.001) high serum levels of total cholesterol (TC) and triglycerides (TG) when compared with the negative control group as recorded in Table 4.

Diets supplemented with dried apricot at 10% level significantly (P <0.01) lowered the elevated serum levels of TC and TG when fed to CCL₄-intoxicated rats when compared with the positive control group as recorded in
Table 2: Effect of feeding diet supplemented with dried apricot at three levels on the initial body weight, final body weight and body weight gain percent (BWG %) in hepatotoxic rats:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial weight (g)</th>
<th>Final weight (g)</th>
<th>Body weight gain (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1) Negative control</td>
<td>184.22 ± 9.71*a</td>
<td>299.48 ± 8.76*c</td>
<td>62.57 ± 0.73*a</td>
</tr>
<tr>
<td>Group (2) Positive control</td>
<td>188.87 ± 4.04*a</td>
<td>228.85 ± 5.22*c</td>
<td>21.17 ± 0.5*a</td>
</tr>
<tr>
<td>Group (3) 5% AP powder</td>
<td>186.66 ± 7.50*c</td>
<td>256.59 ± 5.90*c</td>
<td>37.46 ± 0.75*c</td>
</tr>
<tr>
<td>Group (4) 10% AP powder</td>
<td>188.56 ± 5.50*c</td>
<td>288.5 ± 6.00*b</td>
<td>53 ± 0.67*c</td>
</tr>
<tr>
<td>Group (5) 15% AP powder</td>
<td>188.33 ± 8.36*c</td>
<td>294.36 ± 7.86*c</td>
<td>56.3 ± 0.60*c</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation, (n = 8 for each group).

Values with different superscripts within the column are significantly different at P< 0.05.

Values with similar or partially similar superscripts are non-significant.

Table 3: Effect of feeding diets supplemented with dried apricot at three levels on feed intake and feed efficiency ratio (FER) in hepatotoxic rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean of daily feed intake (g/rat/d)</th>
<th>Feed efficiency ratio (FER)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1) Negative control</td>
<td>24.16</td>
<td>0.176 ± 0.012*a</td>
</tr>
<tr>
<td>Group (2) Positive control</td>
<td>14.6</td>
<td>0.032 ± 0.003*d</td>
</tr>
<tr>
<td>Group (3) 5% AP powder</td>
<td>19.8</td>
<td>0.048 ± 0.009*c</td>
</tr>
<tr>
<td>Group (4) 10% AP powder</td>
<td>21.82</td>
<td>0.098 ± 0.008*b</td>
</tr>
<tr>
<td>Group (5) 15% AP powder</td>
<td>23.4</td>
<td>0.134 ± 0.007*bc</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation, (n = 8 for each group).

Values with different superscripts within the column are significantly different at P< 0.05.

Values with similar or partially similar superscripts are non-significant.

Table 4: Effect of feeding diets supplemented with dried apricot at three levels on the serum level of total cholesterol (TC) and triglycerides (TG) values in hepatotoxic rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TC (mg/dL)</th>
<th>TG (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1) Negative control</td>
<td>99.50 ± 5.6*c</td>
<td>90.50 ± 4.2*d</td>
</tr>
<tr>
<td>Group (2) Positive control</td>
<td>155.00 ± 9.5*b</td>
<td>145.50 ± 8.4*c</td>
</tr>
<tr>
<td>Group (3) 5% AP powder</td>
<td>153.00 ± 9.3*b</td>
<td>144.00 ± 6.2*c</td>
</tr>
<tr>
<td>Group (4) 10% AP powder</td>
<td>137.00 ± 5.9*b</td>
<td>125.50 ± 5.5*c</td>
</tr>
<tr>
<td>Group (5) 15% AP powder</td>
<td>127.50 ± 4.8*b</td>
<td>115.00 ± 4.9*</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation, (n = 8 for each group).

Values with different superscripts within the column are significantly different at P< 0.05.

Values with similar or partially similar superscripts are non-significant.

Table 4. In addition, diets supplemented with dried apricot at 15% level also significantly (P <0.01) lowered the elevated serum levels of TC and TG when fed to CCL₄-intoxicated rats as compared to the positive control group.

Diet supplemented with 5% dried apricot showed no significant changes in the serum values of TC and TG as shown in Table 4.

Results in Table 5 illustrated the effect of different levels of dried apricot on serum values of lipoprotein fractions in hepatotoxic rats.

Intoxication of rats by CCl₄ induced significant (P <0.001) increases in low (LDL) and very low density lipoprotein (VLDL) cholesterol and elevated the high density lipoprotein cholesterol (HDL) when compared with the negative control group as shown in Table 5.

It is clear from Table 5 that feeding CCL₄-intoxicated rats on diets supplemented with dried apricot at 10 and 15% levels significantly (P <0.05) decreased LDL. On the other hand, 10 and 15% levels significantly (P <0.05) increased serum HDL when compared with the positive control group.

Feeding CCL₄-intoxicated rats on diets supplemented with dried apricot 10 and 15% levels significantly (P <0.05) lowered VLDL when compared with the positive control group as shown in Table 5.
Table 5: Effect of feeding diets supplemented with dried apricot at three levels on the serum levels of lipoprotein fractions and atherogenic index in hepatotoxic rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group (1) Negative control</th>
<th>Group (2) Positive control</th>
<th>Group (3) 5% AP powder</th>
<th>Group (4) 10% AP powder</th>
<th>Group (5) 15% AP powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-c (mmol/L)</td>
<td>70.70 ± 5.1a</td>
<td>54.40 ± 4.9a</td>
<td>57.40 ± 3.6c</td>
<td>63.00 ± 4.7b</td>
<td>68.90 ± 3.6e</td>
</tr>
<tr>
<td>LDL-c (mmol/L)</td>
<td>27.00 ± 2.8a</td>
<td>55.20 ± 4.5c</td>
<td>50.80 ± 6.8c</td>
<td>38.90 ± 3.3a</td>
<td>31.60 ± 1.2e</td>
</tr>
<tr>
<td>VLDL-c (mmol/L)</td>
<td>18.10 ± 3.6a</td>
<td>29.10 ± 3.4c</td>
<td>28.80 ± 2.5c</td>
<td>25.10 ± 1.3b</td>
<td>23.00 ± 1.1b</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation, (n = 8 for each group). Values with different superscripts within the column are significantly different at P< 0.05. Values with similar or partially similar superscripts are non-significant.

Table 6: Effect of feeding diets supplemented with dried apricot at three levels on Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) and Alkaline Phosphatase (ALP) in hepatotoxic rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group (1) Negative control</th>
<th>Group (2) Positive control</th>
<th>Group (3) 5% AP powder</th>
<th>Group (4) 10% AP powder</th>
<th>Group (5) 15% AP powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (U/L)</td>
<td>45.5 ± 3.12c</td>
<td>66.0 ± 3.24a</td>
<td>64.0 ± 3.62e</td>
<td>52.5 ± 3.55b</td>
<td>47.4 ± 4.14a</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>35.0 ± 3.31a</td>
<td>56.0 ± 2.33a</td>
<td>53.5 ± 3.73a</td>
<td>45.7 ± 4.52b</td>
<td>37.6 ± 3.12c</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>99.5 ± 4.23d</td>
<td>115.0 ± 3.17c</td>
<td>112.5 ± 3.56d</td>
<td>105.8 ± 2.33d</td>
<td>102.4 ± 3.45d</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation, (n = 8 for each group). Values with different superscripts within the column are significantly different at P< 0.05. Values with similar or partially similar superscripts are non-significant.

Table 7: Effect of feeding diets supplemented with dried apricot at three levels on serum total proteins (TP) and total bilirubin (TBil) in CCL4-intoxicated rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group (1) Negative control</th>
<th>Group (2) Positive control</th>
<th>Group (3) 5% AP powder</th>
<th>Group (4) 10% AP powder</th>
<th>Group (5) 15% AP powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP (g/dL)</td>
<td>8.20 ± 4.27b</td>
<td>3.66 ± 1.05c</td>
<td>3.40 ± 1.09c</td>
<td>6.70 ± 2.43b</td>
<td>7.30 ± 4.14b</td>
</tr>
<tr>
<td>TBil (mg/dL)</td>
<td>0.18 ± 0.01c</td>
<td>0.72 ± 0.05c</td>
<td>0.70 ± 0.04c</td>
<td>0.45 ± 0.02b</td>
<td>0.36 ± 0.01c</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation, (n = 8 for each group). Values with different superscripts within the column are significantly different at P< 0.05. Values with similar or partially similar superscripts are non-significant.

Diet supplemented with 5% of dried apricot caused no significant changes in serum levels of lipoproteins when compared with the positive control group.

It is clear from Table 6 that acute intoxication of rats by CCl4 had significant increases (P <0.001) in serum levels of liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) when compared with the negative control group.

Feeding CCL4-intoxicated rats on diets supplemented with dried apricot at 10 and 15% levels significantly (P <0.01) lowered the high serum values of AST ALT and ALP enzymes when compared with the positive control group as depicted in Table 6.

Diet containing 5% of dried apricot showed no significant changes in serum values of AST, ALT and ALP enzymes when compared with the positive control group as recorded in Table 6.

Results in Table 7 illustrated the effect of feeding diets supplemented with different levels of dried apricot on serum total proteins (TP) and total bilirubin (TBil) in CCL4-intoxicated rats.

Subcutaneous injection of CCL4 in rats significantly (P < 0.001) decreased serum levels of total proteins (TP) and increased total bilirubin (TBil) when compared with the negative control group as shown in Table 7.
Feeding CCl₄ intoxicated rats on diets supplemented with dried apricot at 10 and 15% levels significantly (P <0.01) increased serum levels of TP when compared with the positive control group as recorded in Table 7.

Concerning serum values of total bilirubin (TBil) the results revealed that feeding CCl₄-intoxicated rats on diets supplemented with dried apricot at 10 and 15% levels significantly (P <0.01) decreased TBil when compared with the positive control group as shown in Table 7.

Diet supplemented with 5% of (AP) dried apricot showed no significant changes in serum values of total proteins (TP) and total bilirubin (TBil) in CCl₄-intoxicated rats when compared with the positive control group as depicted in Table 7.

Histopathological Examination: The histopathological examination of liver sections of rats in the negative (normal) control group showed normal histological structure of hepatic lobule as illustrated in Figure 1. Examination of liver sections of rats subcutaneously injected by carbon tetrachloride (CCl₄) in a dose of 1ml/kg (positive control group) revealed presence of karyomegaly, binucleated cells and sporadic cell necrosis (Figure 2).

In CCl₄-intoxicated rats fed on diet containing 5% apricot dried powder, the examination of liver sections showed karyomegaly, sporadic cell necrosis and oval cell hyperplasia. Vacular degeneration of hepatocytes was also detected. Moderate proliferation of fibrous connective tissue restricted to the portal area was seen compared with the positive control group as recorded in Figure 3.

Feeding of Ccl₄ intoxicated rats on diet containing 10% apricot dried powder caused a moderate improvement of pathological lesions where fibrous connective tissue proliferation was minimal (Figure 4). Oval cell hyperplasia in the portal area was very clear and necrosis was more reduced than CCl₄ intoxicated rats fed on basal diet (Figure 5).

Examination of liver sections of rats subcutaneously injected with CCl₄ and fed on diet containing 15% apricot dried powder revealed only mild vacuolar degeneration, oval cell hyperplasia and sporadic cell necrosis (Figure 6). Karyomegaly and binucleated hepatocytes were also seen (Figure 7).

Fig. 1: C.S. of liver of a rat in the control negative (normal) group showing normal histological structure. (H and E stain, X 200)

Fig. 2: C.S. of liver of a rat injected with CCl₄ showing Karyomegaly, binucleated cell and sporadic hepatic cell necrosis. (H and E stain, X 400)
Fig. 3: C.S. of liver of a rat injected with CCl₄ and fed on diet containing 5% apricot dried powder showing karyomegaly and sporadic cell necrosis. (H and E stain, X 400)

Fig. 4: C.S. of liver of a rat injected with CCl₄ and fed on diet containing 10% apricot dried powder showing focal area of necrosis. (H and E stain, X 200)

Fig. 5: C.S. of liver of a rat injected with CCl₄ and fed on diet containing 10% apricot dried powder showing few necrotic cells. (H and E stain, X 400)

Fig. 6: C.S. of liver of a rat injected with CCl₄ and fed on diet containing 15% apricot dried powder showing karyomegaly and inucleated hepatocytes. (H and E stain, X 200)
DISCUSSION

Concerning Feed intake (FI) and body weight gain percent (BWG%) rat group intoxicated with CCl₄ revealed significant decrease in final weight and weight gain percent compared to control negative group. These results were in agreement with Balamurugan and Muthusamy [23] who confirmed our results. The decrease in body weight of hepatotoxic rats might be due to the reduction in feed intake caused by CCl₄ poisoning which led to loss of appetite of rats. Moreover, the beneficial effect of antioxidant administration against CCl₄ poisoning with respect to body weight observed in the present study confirms previous results obtained by Aneja et al. [24] who concluded that feeding rats with antioxidants could play an important role as a prophylactic against the toxic effects of CCl₄. Ozturk et al. [25] found that dried apricot significantly increase final body weight compared to control positive group due to apricot antioxidant nutrient (beta-carotene) content which neutralize the toxic effect of CCl₄. Also Yilmaz et al. [26] determined that there was a statistical significant incensement in average daily chow consumption of an additional 10% sun dried organic apricot (SDOA) than the control group of the female rats, it might be due to phytoestrogens (isoflavones) which is a content of apricot and that can be pointed out as a result of the existing different hormone which is originated from the estrogenic effect which could cause an increase on appetite.

Liver is the most important organ of the animal body and is highly affected primarily by toxic or xenobiotic agents [27]. Results obtained in the present study showed that there was a significant (p<0.05) increase in the relative liver weight in hepatotoxic rats when compared to the negative control group. This result was consistent with previous study reported by Lin and Lin [28] who demonstrated that injection of CCl₄ in rats to induce liver fibrosis lead to increase in liver weight. Imafidon et al. [29] who reported that relative organs weight were significantly increased after injection with CCl₄. Results of our study showed that feeding dried apricot to hepatotoxic rats showed a significant decrease in relative liver weight compared with control +ve group, this finding was in consistent with that reported by Soni et al. [30] and Ozturk et al. [25]. These results could be explained on the basis that feeding dried apricot had beneficial effects on CCl₄-induced liver steatosis and damage probably due to its antioxidant nutrient (beta-carotene) contents and high radical-scavenging capacity.

In the current study the results revealed that intoxicated rats with CCl₄ resulted in significant increase in serum values of total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) accompanied with a significant decrease in high density lipoprotein cholesterol (HDL-c) level as compared to the negative control group. Our results in agreement with El-Habibi et al. [31] and Al-Dosari [32]. Boll et al. [33] who reported that there was an increase in the values of cholesterol, triglycerides and free fatty acids in plasma and tissues. Carbon tetrachloride CCl₄ increases the synthesis of fatty acids and triglycerides from acetate. This could be due to the transport of acetate into the liver cell, resulting in increased substrate (acetate) availability. In CCl₄ toxicity, the synthesis of cholesterol is also increased.

Lieber [34] stated that CCl₄ intoxication is similar to hepatitis in case of the triglycerides catabolism. This situation could be also attributed to the reduction of lipase activity, which could lead to an increase in triglyceride by decreasing its hydrolysis. On the other hand, it can be assumed that hypercholesterolemia in CCl₄...
intoxicated rats was resulted from damage of hepatic parenchyma cells that lead to disturbance of lipid metabolism in liver as well as increasing in low density lipoprotein cholesterol (LDL-c) production and very low density lipoprotein cholesterol (VLDL-c) secretion from the liver and hepatic LDL receptor activity.

Apricot is rich in phytosterols, which is widely reported to reduce serum cholesterol value in animals and humans [35]. Our results revealed that pretreatment of rats with dried apricot resulted in significant improvement in the tested lipid profile parameters, that could be attributed to increase the inhibition of intestinal absorption of cholesterol, interference with lipoprotein production which increased expression of hepatic LDL receptor and their protection, leading to an increase the removal of LDL-c from the blood and its increased degradation and catalolism of cholesterol from the body. All these events either individually or in combination lead to decrease in serum LDL-c levels, which reduced serum total cholesterol value during pretreatment [36].

According to a study conducted by Vanstone et al. [37] the hypocholesterolemic effect of apricot may be explained by two mechanisms including the inhibition of (a) cholesterol absorption and (b) hepatic cholesterol esterase. On the other hand, apricot has been shown to lower LDL-c cholesterol equivalently in hypercholesterolemic persons by suppressing cholesterol absorption. Plant sterols decreased the incorporation of dietary and biliary cholesterol into micelles and this lowers cholesterol absorption and ultimately leads to decreased serum LDL-c values [38].

Carbon tetrachloride (CCl4) is considered as a direct hepatotoxin which produces centrilobular necrosis and steatosis in liver [39]. In the assessment of liver damage by CCl4, the determination of enzyme activities such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) is largely used. Necrosis or membrane damage releases the enzyme into circulation and hence it can be measured in the serum. High levels of AST indicates liver damage, such as that caused by viral hepatitis as well as cardiac infarction and muscle injury, AST catalysis the conversion of alanine to pyruvate and glutamate and is released in a similar manner. Therefore ALT is more specific to the liver and is thus a better parameter for detecting liver injury. Elevated activities of serum enzymes are indicative of cellular leakage and loss of functional integrity of cell membrane in liver. Serum alkaline phosphatase (ALP), total bilirubin (TBil) and total protein (TP) activities on other hand are related to the function of hepatic cell. Increase in serum activitie of ALP is due to increased synthesis, in presence of increasing biliary pressure [40]. In the present study, the hepatotoxicity of CCl4 in rats was confirmed by a significant elevation of AST, ALT, ALP and total bilirubin values. In addition, CCl4 intoxication produced a significant reduction in plasma total protein value. This may be due to release of these enzymes from the cytoplasm into the blood rapidly after cellular damage and a reduction in hepatic protein synthesis. Liu et al. [41] reported that elevation of AST, ALT and ALP in response to CCl4 could be attributed to hepatic structural damage because these enzymes are normally localized to the cytoplasm and are released into the circulation after cellular damage has occurred.

Histopathological observations of the liver of CCl4-administered rats showed revealed presence of karyomegaly, bi-nucleated cells and sporadic cell necrosis. Individual hepatic cell necrosis exhibited karyopyknosis and eosinophilic cytoplasm were seen. Fibrous connective tissue proliferation in the portal area, interlobular septa and hepatic capsule was evident. Hyperplasia of the bile duct epithelium was very clear as well. These results were in harmony with the previous data reported by previous findings that CCl4 causes necrosis, fibrosis [42], mononuclear cell infiltration [43], steatosis and degeneration of hepatocytes, increase in mitotic activity [42] and cirrhosis [44] in liver. It has also been reported that CCl4 causes apoptosis in liver. Increased activity levels of AST, ALT and ALP in the serum of the present study, reveal CCl4 induced mixed hepatic cellular type injury [45].

Feeding dried apricot at levels of 10 and 15% to hepatotoxic rats during the experimental period (8 weeks) showed significant decreases of AST, ALT, ALP and total bilirubin values. In addition there was a significant increase in plasma total protein value compared to control positive group. The present results agreed with the results obtained by Ramadan et al. [46], Ismet et al. [40] and Yilmaz et al. [26] who reported that the increase in apricot supplementation rates caused a decrease of serum ALT, AST and ALP I activities. These changes may be due to the antioxidant content of dried apricot which contain high amounts of phytochemicals, tocopherols and carotenoids which may play a role in scavenging free radicals [46] or it may prevent increases of serum aminotransferase increase in the early periods of liver damage. Sugiera et al. [47], Liu [48] and Kok et al. [49] indicated that apricot feeding prevented lipid peroxidation and decreased oxidative stress. Their health-promoting properties are due to high vitamin, phytochemical and
fiber content. However, the isolated single phytochemical does not exert the same beneficial health effect. It seems that combinations of phytochemicals are likely to show beneficial effects by their overlapping and complementary mechanisms. Thousands of phytochemicals are present in whole foods. Apricot is a phytochemical- and vitamin rich fruit. The synergistic effect of these compounds could probably have played an important role in apricot’s hepatoprotective effect.

The biochemical results of our study were confirmed by histopathological findings, which seen in liver sections. The histological findings of liver of treated rats with dried apricot at levels of 10 and 15% showed almost completely normal structure with mild fibroblastic proliferation and sporadic cell necrosis. Karyomegaly and binucleated hepatocytes were also seen. Oval cell hyperplasia in the portal area was very clear and necrosis was more reduced than CCl4 intoxicated rats fed on basal diet, thus may be explained by antioxidant activity of dried apricot that may be attributed to its constituents of high vitamin, phytochemical and fiber content. These histological findings agreed with the study of Yilmaz et al. [26] who demonstrated that Pretreatment with apricot significantly improved the structure of hepatic cells.

In conclusion, the results suggested that dried apricot alleviated hepatorenal toxicity induced by CCl4. Thus could be attributed to their active biochemical compounds that have potent antioxidant activity.

REFERENCES


