Hepatoprotective Activity of Aqueous and Ethanol Extract of *Lippia adoensis* Leaf Against Carbon Tetrachloride-Induced Hepatotoxicity in Mice

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Abstract: Liver disease is one of the fatal diseases. Medicinal plants may serve as one of the best sources of remedies for treatment of liver disease. Identification of a potential therapeutic agent for protection of liver from hepatotoxins provides a useful way for the prevention of liver related illnesses. The aim of the present study was, therefore, to investigate the hepatoprotective activity of 80% ethanolic and aqueous extract of leaves of *Lippia adoensis* against carbon tetrachloride induced liver injury in mice. Mice were pretreated with extract of *Lippia adoensis* (200 & 400 mg/kg bw. po) for 7 days and then challenged with *CCl₄* (0.2 ml/100 gm p. o) on the 7th day. Serum biomarkers (AST, ALT, ALP and total bilirubin, total protein and albumin) were estimated in all the study groups. Histopathological examination was also carried out for all groups of mice. *CCl₄* significantly (P < 0.001) increased the AST, ALT, ALP and total bilirubin levels and decreased the level of total protein and albumin indicating hepatic damage. Pretreatment with the extract of *Lippia adoensis* (200 & 400 mg/kg) produced significant (P < 0.001) hepatoprotective effects as evidenced by decreased serum enzymes (AST, ALT, ALP) and serum bilirubin and increase the level of total protein and albumin as well as by histopathological findings of the liver. Histopathological examination of the liver tissues of *CCl₄* group represented the presence of marked foci of mononuclear infiltration in the hepatic parenchyma tissue, sinusoid and around central vein, as well as disorganization of hepatic plates, while pretreatment with extract of *Lippia adoensis* overcome most of these changes to normal histological architecture of the liver. Body weights of *Lippia adoensis* extract treated groups increased significantly (P < 0.001) as compared to carbon tetrachloride treated group. The absolute and relative liver weights of extracts treated mice decreased significantly (P < 0.001) as compared to those treated with *CCl₄*. The results obtained from both ethanolic and aqueous extract of *Lippia adoensis* were comparable with those of the standard drug, Silymarin. It can be concluded from the present study that both ethanolic and aqueous extracts of *Lippia adoensis* have hepatoprotective effect.

Keywords: *Lippia adoensis*, Aqueous Extract, Ethanol Extract, Hepatoprotective, *CCl₄*, Silymarin, AST, ALT, ALP, Bilirubin, Protein, Albumin and Mice

1. Introduction

Liver is the largest organ in the body and plays a significant role in protecting various biological function and help in detoxification and excretion of various endogenous and exogenous compounds (Mohamedet *et al.*, 2010). The
liver is often the target organ for chemically induced injuries. Many oxidative reactions produce reactive metabolites that can induce lesions within the liver. The types of injury to the liver depend on the type of toxic agent, the severity of intoxication, and the type of exposure, whether acute or chronic (Comfort et al., 2013; Singh et al., 2011).

*Lippia adoensis* included under Verbenaceae that is a large family with about 70 to 80 genera and over 3,000 species; distributed throughout the world mainly in the tropics and temperate regions. *Lippia* is a genus with 200 species in tropical Africa and America (Toshihiro et al., 1992). In Ethiopia, the family is represented by 9 genera and 30 species. *Lippia adoensis* (locally known as “Kesse”) is a shrub having a height of 1 to 3 meters. Two varieties of *Lippia adoensis* are recognized in Ethiopia, the wild variety (*var. adoensis*) and the cultivated variety (*var. koseret*). The fragrant leaves are used by the Gurage and Oromo tribes as one of the condiments in the preparation of spiced butter. The special taste and flavor of the “Gurage Kitfo” is imparted by the leaves (Toshihiro et al., 1992). In Ethiopia, the wild variety (*var. adoensis*) is used for washing kitchen utensils to impart fresh and spicy fragrance (Abegaz et al., 1993). The chemical compositions of *Lippia adoensis* investigated so far are essential oils. The oils were predominantly monoterpenoids with minor sesquiterpenoid fraction. In one study, out of more than 10 compounds isolated, linalool comprised 81.30% and 94.56% of the leaf and flower oils, respectively (Asres and Bucar, 2002). It is well documented that *Lippia adoensis* is one of the rich sources of flavonoids, Phenolics, tannins, saponins and alkaloids (Riot et al., 2005). The leaves of *L. adoensis* are used in Ethiopian traditional medicine for the treatment of various skin diseases including eczema and superficial fungal infections (Asres et al., 1986). Review of literature revealed that this rare medicinal plant remained unexplored for many of its claimed pharmacological activities. The present study was conducted to establish the use of *Lippia adoensis* as hepatoprotective against CCl$_4$ induced hepatotoxicity in mice.

2. Methodology

2.1. Collection of Plant Materials

Fresh leaves of *L. adoensis* were collected in Addis Ababa, Ethiopia, on January 18, 2014. Plant identification and authentication was done with the help of local florists. The specimen has been preserved in AAU herbarium with the voucher number of 084908.

2.2. Preparation of Plant Extracts

One kilogram of dried powder plant material was macerated in ethanol (80%) in a ratio of 1:1. It was then filtered and the filtrated extract was then concentrated by evaporation using Rota vapor at temperature not exceeding 40°C. Then the resulting aqueous residue was placed in an oven for about 48 hours at a temperature of 40°C. One kilogram of dried powder plant material was macerated in water in a ratio of 1:1. The mixture was then filtered and the filtrated extract was lyophilized for 24 h. The resulting powder was stored in amber colored glass bottle in desiccators over silica gel for use in subsequent experiments (Bimlesh et al., 2011).

2.3. Experimental Animals

A total of 42 healthy male mice weighing 25-35 gram were obtained from animal house of department of pharmacology, School of medicine, AAU and Ethiopian Public Health Institute (EPHI) were used throughout the study. They were kept under standard environmental conditions at 22±3°C with 12:12 hour light–dark cycle in ventilated plastic cages. The animals were housed in steel mesh cages, (6 per cage) and had a free access to feed with a standard pellet diet and water ad libitum. The animals were acclimatized to laboratory conditions for one week prior to experimentation.

3. Experimental Design

3.1. Hepatoprotective Activity

The body weights of all mice were recorded at the beginning of the experiment. Experimental mice were divided in seven groups (n=7) of six mice/group. The animals were fasted overnight before the initiation of the study. Group I served as normal control which received vehicle (5% gum acacia; 1 ml/kg, p. o) orally daily for seven days. Group II received CCl$_4$ (0.2 ml/100 gm p. o) on seventh day. Group III served as standard and received silymarin (100 mg/kg p. o) daily for seven days and thirty minutes post dose of silymarin mice received CCl$_4$ (0.2 ml/100 gm p. o.) on the seventh day. Group IV and Group V were treated with the aqueous extract of *L. adoensis* at the doses of 200 mg/kg and 400 mg/kg, respectively in 5% aqueous gum acacia orally daily for seven days. Group Vland Group VII were treated with the ethanolic extract of *L. adoensis* at the doses of 200 mg/kg and 400 mg/kg, respectively in 5% aqueous gum acacia orally daily for seven days. Thirty minutes post dose of extract administration, animals received CCl$_4$ at the dose of 0.2 ml/100 gm orally(Sunita et al., 2014; Sabreena et al., 2014; Showket et al., 2014).

3.2. Blood Collection

The blood sample from each mouse was collected separately in sterilized dry centrifuge tubes by cardiac puncture and allowed to coagulate for 10 minutes at 37°C. The clear serum was separated at 2500 rpm for 10 minutes. The serum collected was used for biochemical analyses. All biochemical analyses were carried out within 24 hours of serum separation. (Maliha and AL-Marzoq, 2014; Iyanda and Adeniyi, 2014).
3.3. Histopathological Examination

After collection of blood sample, the mice were scarified and then the liver was excised from the animals and washed with normal saline. The absolute weight of liver tissue was measured. The tissues of liver were fixed in 10% formalin and processed separately for histopathological observation. The microscopic slides were examined under a microscope by a pathologist who was blind to the protocol of the study (Alaezi et al., 2014; Bhaskara and Mukalel, 2014).

3.4. Statistical Analysis

The results were expressed as means ± standard errors of mean (SEM). The data were analyzed by one way analysis of variance (ANOVA). P < 0.05 was considered statistically significant. The statistical analysis was carried out using the SPSS program (version 21.0).

4. Results

4.1. Yields of the Aqueous and 80% Ethanol Extracts

Leaves of Lippia adoensis were extracted with aqueous and 80% ethanol using maceration technique and these extracts were used for investigation of hepatoprotective activity. The percentage yields of these extracts are given in Table 1. The yields of aqueous and ethanol extracts were found to be 16.3% and 12.7%, respectively.

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Extracts</th>
<th>Parts used</th>
<th>Percentage yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lippia adoensis</td>
<td>Aqueous</td>
<td>Leaves</td>
<td>16.3</td>
</tr>
<tr>
<td>Lippia adoensis</td>
<td>80% Ethanol</td>
<td>Leaves</td>
<td>12.7</td>
</tr>
</tbody>
</table>

4.2. Limit Dose Test

Limit test was performed following OECD (Organization of Economic Co-Operation Development) guidelines–423. The purpose of this study was to allow selection of the appropriate starting dose for the main study. The animals did not show any signs of toxicity and behavioral changes after 24 hrs and 72 hrs. The oral LD50 was estimated to be above 3000mg/kg.

4.3. Effects of Lippia adoensis Extract on Body Weight, Liver Weight and Relative Liver Weights Ratio in CCl4 Intoxicated Mice

Both aqueous and ethanol leaves extracts prevented reduction significantly (p<0.01) in the bodyweights of mice treated with carbon tetrachloride at both doses comparable to that of the standard as shown in table 2. The same table shows a significant decrease in both absolute and relative liver weight with both doses of both extracts comparable to those of the standard.

<table>
<thead>
<tr>
<th>Groups Treatment</th>
<th>Body weight (gm) Initial</th>
<th>Final</th>
<th>Body weight Change</th>
<th>Absolute Liver weight(gm)</th>
<th>Relative liver Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>29.00 ± 0.93</td>
<td>32.33 ± 0.88</td>
<td>2.83 ± 0.60</td>
<td>1.47±0.05</td>
<td>4.53±0.084</td>
</tr>
<tr>
<td>CCl2ml/kg</td>
<td>32.17±0.74*</td>
<td>28.33 ± 0.76**</td>
<td>2.88±0.87*</td>
<td>1.69±0.07*</td>
<td>7.97±0.43#</td>
</tr>
<tr>
<td>Sylimarin100mg/kg</td>
<td>29.83±0.48***</td>
<td>32.50 ± 0.43**</td>
<td>2.67±0.33**</td>
<td>1.50±0.03**</td>
<td>4.52±0.06**</td>
</tr>
<tr>
<td>Aqueous extract200mg/kg</td>
<td>28.83 ± 0.79*</td>
<td>30.83±0.65***</td>
<td>1.83±0.30**</td>
<td>1.76±0.06**</td>
<td>5.53±0.23**</td>
</tr>
<tr>
<td>Aqueous extract400mg/kg</td>
<td>28.33 ± 0.67*</td>
<td>30.67±0.56***</td>
<td>2.33±0.49**</td>
<td>1.69±0.07**</td>
<td>5.50±0.28**</td>
</tr>
<tr>
<td>Ethanol extract200mg/kg</td>
<td>27.83±0.83**</td>
<td>30.67±0.88***</td>
<td>2.83±0.40**</td>
<td>1.71±0.10**</td>
<td>5.62±0.42**</td>
</tr>
<tr>
<td>Ethanol extract400mg/kg</td>
<td>29.17±0.7031*</td>
<td>31.83±0.83</td>
<td>2.83±0.48**</td>
<td>1.65±0.16**</td>
<td>5.20±0.57**</td>
</tr>
</tbody>
</table>

Values are expressed as means ± standard error of means (SEM) of six mice treated for 7 days.

* P<0.01, ** P<0.001, *P<0.01, *** P<0.05 were statistically significant. Symbols represent statistical significance;# significantly different from control

4.4. Effects of Lippia adoensis Leaves Aqueous and Ethanol Extract on AST, ALT, ALP, Total Bilirubin, Albumin and Total Protein Serum Levels

The serum levels of AST, ALT, and ALP significantly (P<0.001) increased in carbon tetrachloride treated mice; as compared to those in the control mice (table 3). Pretreatment with 200mg/kg and 400mg/kg both ethanolic and aqueous extracts of Lippia adoensis leaves significantly reduced (P<0.001) the levels of AST, ALT and ALP after carbon tetrachloride administration (table 3). The standard drug, silymarin also significantly (P < 0.001) reduced the serum levels of AST and ALP as shown in table 3.

The level of total bilirubin in serum significantly(P<0.001) increased in carbon tetrachloride treated mice compared to that of the normal control mice as shown in table 3. The same table shows that both doses of Lippia adoensis ethanolic and aqueous extracts (200mg/kg) reduced the levels of total bilirubin significantly (P < 0.001) The level of serum total protein significantly (P<0.001) reduced in carbon tetrachloride treated mice, while Administration of both doses of both extracts significantly (P<0.001) increased the serum total protein level comparable to that of the standard (table 3).

The same table shows the level of albumin significantly (P<0.001) reduced in carbon tetrachloride treated mice; while both doses of both extracts increased the level significantly (P<0.001) comparable to that of the standard.
### Table 3. Effects of extracts of Lippia adoensis on CCl₄ induced liver damage in mice.

<table>
<thead>
<tr>
<th>Sr. no</th>
<th>Group</th>
<th>Dose (po)</th>
<th>AST (IU/L)</th>
<th>ALT (IU/L)</th>
<th>ALP (IU/L)</th>
<th>Total Protein (gm/dl)</th>
<th>Total Bilirubin mg/dl</th>
<th>Albumin mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>Vehicle(5%Acacia)</td>
<td>104.17± 4.41</td>
<td>126.67±1.61</td>
<td>201.17±4.52</td>
<td>6.75± 0.21</td>
<td>1.15±0.13</td>
<td>2.18 ±0.15</td>
</tr>
<tr>
<td>2</td>
<td>CCl₄ control</td>
<td>2ml/kg</td>
<td>251.83±3.46*</td>
<td>286.83±2.52*</td>
<td>446.50±3.67*</td>
<td>4.63±0.15*</td>
<td>4.48 ±0.12*</td>
<td>1.67±0.20*</td>
</tr>
<tr>
<td>3</td>
<td>Silymarin+ CCl₄</td>
<td>100mg/kg</td>
<td>112.50±3.24**</td>
<td>129.83±2.02**</td>
<td>220.67±2.95**</td>
<td>6.67±0.12**</td>
<td>1.17±0.07**</td>
<td>2.47±0.17**</td>
</tr>
<tr>
<td>4</td>
<td>Aqueous extract + CCl₄</td>
<td>200mg/kg</td>
<td>135.50±4.27**</td>
<td>143.67±2.44**</td>
<td>257.83±2.75**</td>
<td>6.17±0.11**</td>
<td>2.05±0.14**</td>
<td>2.62±0.09**</td>
</tr>
<tr>
<td>5</td>
<td>Aqueous extract + CCl₄</td>
<td>400mg/kg</td>
<td>127.0±1.79**</td>
<td>138.33±3.29**</td>
<td>225.5±2.44**</td>
<td>6.23±0.09**</td>
<td>1.983±0.25**</td>
<td>2.63±0.07**</td>
</tr>
<tr>
<td>6</td>
<td>Ethanolic extract + CCl₄</td>
<td>200mg/kg</td>
<td>128.83±2.89**</td>
<td>141.83±2.76**</td>
<td>233.67±3.45**</td>
<td>6.15±0.11**</td>
<td>2.22±0.11**</td>
<td>2.65±0.085**</td>
</tr>
<tr>
<td>7</td>
<td>Ethanolic extract + CCl₄</td>
<td>400mg/kg</td>
<td>126.17±4.38**</td>
<td>140.50±2.01**</td>
<td>227.67±3.05**</td>
<td>6.22±0.08**</td>
<td>2.10±0.13**</td>
<td>2.67±0.11**</td>
</tr>
</tbody>
</table>

Values are mean ± S. E. M, (n=6); P < 0.001
Symbols represent statistical significance * considered significantly different at P < 0.001 when compared with normal control group; ** considered significantly different at P < 0.001 when compared with CCl₄ alone control group.

### 4.5. Effect of Lippia adoensis Extracts on Histopathology

Histopathological analysis of liver sections revealed that carbon tetrachloride (0.2 ml/100 gm p. o) intoxication caused marked foci of mononuclear infiltration in the hepatic parenchyma tissue, sinusoid and around central vein, as well as disorganization of hepatic plates in contrast to the central veins and thin sinusoids observed in normal mice (Figure 1). In contrast, in carbon tetrachloride treated mice, there was massive necrosis throughout the liver, in some areas whole lobules being degenerated, in others the more central hepatic cells showing the greater disintegration (Figure 2). Pretreatments with Lippia adoensis extracts at both doses resulted in normal hepatic cells, central vein and sinusoids with no necrosis and foci of mononuclear infiltration comparable to that observed with the standard as shown in figure 3.

In the liver section from 200 mg/kg Lippia adoensis aqueous extract pretreated mice hepatic cells, central vein and sinusoids were normal, except the presence of a minimal focus of mononuclear infiltration at the periphery (Figure 4); whereas, in the one from 400 mg/kg Lippia adoensis aqueous extract pretreated mice there was a marked protection with normal hepatic cells, central vein and sinusoids (Figure 5). Similarly, in the liver section from 200 mg/kg Lippia adoensis ethanolic extract pretreated mice there was a marked protection with normal hepatic cells, central vein and sinusoids (Figure 6).

There was also no histopathological change in the sections of the liver from 400 mg/kg Lippia adoensis ethanolic extract pretreated mice with normal hepatic cells, central vein and sinusoids (Figure 7). The histological appearance of the Lippia adoensis extract pretreated groups was quite similar to that of the control group, and tissue damage and necrosis were of less extent in Lippia adoensis extract treated group than the CCl₄ group.

*Figure 1. Section of liver from the control group showing normal architecture of the hepatic lobule with no histopathological change H & E staining (x100).*
Figure 2. Liver section from mice treated with CCl₄ at a dose of 0.2ml/100 gm p. o; bw showing a focal mononuclear infiltration (arrow) H & E staining (x100).

Figure 3. Liver section from mice treated with silymarin and CCl₄ showing normal architecture of the hepatic lobule with no histopathological change H & E staining (x100).

Figure 4. Liver section from mice treated with 200mg/kg Lippia adoensis aqueous extract and CCl₄ showing normal architecture of the hepatic lobule with minimal focus of mononuclear infiltration at the periphery (arrow) H & E staining (x100).
Figure 5. Liver section from mice treated with 400 mg/kg Lippia adoensis aqueous extract and CCl₄ showing normal architecture of the hepatic lobule with no histopathological change H & E staining (x100).

Figure 6. Liver section from mice treated with 200 mg/kg Lippia adoensis ethanolic extract and CCl₄ showing normal architecture of the hepatic lobule with no histopathological change H & E staining (x100).

Figure 7. Liver section from mice treated with 400 mg/kg Lippia adoensis ethanolic extract and CCl₄ showing normal architecture of the hepatic lobule with no histopathological change H & E staining (x100).
5. Discussion

Medicinal plants are getting great attention as important sources of bioactive substances, with health beneficial effects. However, a great limitation to the use of medicinal plants is the issue of safety and toxicity. Liver damage is a widely used indicator of toxicity of medicinal plants in vivo (Kadejo et al., 2012; Manju et al., 2014).

The significant increase in body weight and decrease in absolute and relative liver weights in extract pretreated mice indicates that the plant extract protects liver from hepatotoxic agents. The results from the present study moreover reveal a relationship between body weight/absolute:relative liver weights and liver function. Muhammad et al. and Douhri et al. reported similar results those of the present study. Bhaargavi et al. demonstrated that in hepatotoxicity, liver weight increases generally as a consequence of necrosis and fibrosis or hypertrophy of the liver and body weight decreases due to infiltration of hepatic parenchyma, disorganization of hepatic plates and fatty change. The alterations in the body weight and the liver weight in mice after CCl₄ administration were considered to result from direct toxicity of the liver and indirect toxicity related to liver damage (Andreia et al., 2013). Change in relative liver weight is a valuable index of the extent of acute hepatic damage (Douhri et al., 2014).

The aminotransferases (ALT, AST), ALP and bilirubin are among serum biomarkers of hepatic function, with their increase in the serum indicating hepatic damage (David et al., 2014), where as decreased level of total protein and albumin in the serum indicating hepatic damage (Kanwal et al., 2012). Pretreatment of normal mice with Lippia adoensis did not result in any toxicity or adverse effects as indicated by the insignificant change in serum levels of ALT, AST, and ALP, total bilirubin, total protein and albumin in liver damage. Results from the present study confirmed that CCl₄ induced hepatotoxic effects manifested by a significant increase in activity of liver function marker enzymes ALT, AST, ALP and bilirubin in the serum of CCl₄ treated mice, whereas total protein and albumin in the serum of CCl₄ treated mice decreased significantly. These observations are in accordance with those in similar studies (Senthilkumar et al., 2014; Isha et al., 2014; Mary et al., 2014). In the present study, the levels of bilirubin and total protein and albumin were restored to the normal values after administration of the plant extract indicating its hepatoprotective action. This effect was found to be comparable to that of standard drug (silymarin). The results generally suggest that the imbalanced antioxidant system in liver treated with carbontetrachloride is normalized by the protective effect of L. adoensis extract.

Lippia adoensis pretreatment of CCl₄ treated mice significantly reduced the elevated levels of ALT, AST, ALP and bilirubin. The diminished levels of these serum biomarkers may be attributed to the stabilizing effect of the Lippia adoensis phytochemical constituent(s) and various active ingredients on the plasma membrane of the hepatocytes, probably brought about by the stimulation of hepatocellular protein synthesis and ability to induce microsomal enzymes either by accelerating the excretion of CCl₄ or by inhibition of oxidative stress induced by CCl₄(Farhan et al., 2012; Sagar et al., 2012).

Food rich in plant bioactive compounds and polyphenols and flavonoids in particular may exert beneficial effects towards human health (Francesco et al., 2011). Health benefits of phytochemicals, especially antioxidant properties of phenolic compounds, which is known to exert preventive activity against degenerative diseases, inflammation and allergies via antioxidant, proteins and enzymes neutralization or modulation mechanisms (Tulay et al., 2014).

Among plants containing natural antioxidants, Lippia adoensis has attracted particular interest due to a high content of biologically active compounds (Riotet et al., 2005). It has been considered to play an important dietary antioxidant role in the prevention of oxidative damage in living system (Tadewos et al., 2014).

CCl₄ induced hepatic damage observed was confirmed by histopathological examination of the CCl₄ treated mice which revealed severe hepatic degeneration and marked foci of mononuclear infiltration of hepatic parenchyma tissue and around central vein, disorganization of hepatic plates and tissue necrosis (Snehal et al., 2014).

Carbontetrachloride is a widely used experimental hepatotoxicant biotransformed by cytochrome P-450 system to produce trichloromethyl free radical, which in turn covalently binds to cell membranes and organelles to elicit lipid peroxidation, disturb Ca²⁺ homeostasis and finally result in cell death (Muhammad et al., 2014). Liver damage induced by carbontetrachloride is a classical model for screening the hepatoprotective activity (Showket et al., 2014).

Histopathological findings of liver samples were in agreement with the results obtained in serum biochemical studies, indicating that L. adoensis extract is able to protect carbontetrachloride induced hepatotoxicity. Phenolics and flavonoids display a wide range of biological and pharmacological properties, and they normally scavenge the free radicals and play an essential role in preventing oxidative stress (Kutaiba et al., 2014).

The outcome of the present investigation indicates that treatment with L. adoensis was effective in inhibiting the hepatotoxic effect of carbontetrachloride in vivo models, most likely because of high content of flavonoids, alkaloids, phenolics, tannins and saponins and active principle (Amita et al., 2014). However, the precise molecular mechanism by which L. adoensis mediates its hepatoprotective action is still not clear. In the present study, Carbontetrachloride treatment produced centrilobular necrosis (zone 3), marked foci of mononuclear infiltration to hepatic parenchyma tissue, sinusoid and around central vein, disorganization of hepatic plates (Gayathiri et al., 2012).
Pretreatment with *Lippia adoensis* extract protected hepatic architecture and liver tissue from marked foci of mononuclear infiltration of hepatic parenchyma tissue, sinusoid and around central vein, as well as disorganization of hepatic plates and tissue necrosis, by preventing the toxic chemical reaction, oxidative stress, molecular changes in the liver tissues ultimately leading to necrosis. Similar reports were observed from some other plants including *veronica ciliatifisich* (Li et al., 2014), *Mung Bean* (Norlaiy et al., 2013), *Deinococcus radiodurans* (Cheng et al., 2014) and *Lumnitzera racemosa* (Sundaram and Murugesan, 2011).

Histopathological changes indicating liver damage after CCl₄ administration has been reported in the previous findings that CCl₄ causes necrosis (Sampath et al., 2013), fibrosis (Jamaliah et al., 2014), mononuclear cell infiltration (Jamaliah et al., 2014), steatosis and degeneration of hepatocytes, in the liver and also CCl₄ causes apoptosis in liver (Sampath et al., 2013). Therefore, histopathological findings in the liver due to CCl₄ administration are in agreement with previous studies.

Hepatoprotective drugs may play a role in the process of regeneration, prevention of fibrosis, or formation of nodules which may be expressed in the long term of the drug (Elsohafy et al., 2013). This study, however, showed marked foci of mononuclear infiltration to hepatic parenchyma tissue, sinusoid and around central vein, disorganization of hepatic plates and tissue necrosis by hepatotoxic (CCl₄) and prevention of such changes and restoration to normal by *Lippia adoensis* extracts. In conclusion, the present results show that *Lippia adoensis* leaves ethanolic and aqueous extracts at the doses of 200mg/kg and 400mg/kg have potential hepatoprotective effect.

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References


