Effect of *Artemisia deserti* flowering taps extract on liver in male rats

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**ABSTRACT:** Liver transaminases: aspartate amino transferase (AST) and alanine amino transferase (ALT) are biomarkers of liver damage in a patient. High-density lipoprotein (HDL) and low-density lipoprotein (LDL) are from the five significant groups of lipoproteins which allow lipids to be transported within the water-based blood flow. Multiple plants are used for the treatment of liver diseases. Therefore, the aim of this study is to evaluate the effects of extracts from *Artemisia deserti* extract on liver. Artemisia is a large, diverse genus of the family Asteraceae. In this study after collecting and provision plant, they were dried under shade and ground into fine powder using electric blender, then, 20 gr of flower powder were extracted with 150 mL 80% ethanol by Soxhlet extraction for 8 hours. The dried extracts were stored at 4 °C until used. The animals were divided into three groups. Group 1 was injected with saline, group 2 and 3 were injected with extract 100 mg/kg and 200 mg/kg respectively. The animals were anesthetized and the AST, ALT, ALP, LDL and HDL were assayed. Also the liver tissue was separated and pathological changes were studied. No significant changes in liver enzymes were observed in all three groups. But, the flower extract of *A. deserti* cause changes in the liver tissue. The results are shown that the histopathological change probably due to the existing of artemisinin at extracts. It also seems liver disorders is resolved with time.

**Keywords:** *Artemisia deserti*, extract, liver, AST, ALT.

**INTRODUCTION**

The liver, is a necessary organ present in vertebrates and some other animals. It has a wide range of functions, including detoxification, protein synthesis, and production of biochemicals necessary for digestion, glycogen storage, decomposition of red blood cells, hormone production (Thapa and Walia, 2007). Liver transaminases [AST/ALT (SGOT/SGPT)] are biomarkers of liver damage in a patient with some degree of undamaged liver function other sources include transaminases. AST and ALT are liver enzymes included in amino acid metabolism (Kabir et al., 2008; Lee et al., 2012).

ALT is discover in kidney, heart, muscle and much concentration in liver compared with other tissues of the body. AST is entirely in highest concentration in heart compared with other tissues of the body such as liver, skeletal muscle and kidney. Alkaline phosphatase (ALP) is present in mucosal epithelia of small intestine, proximal convoluted tubule of kidney, bone, liver and placenta (Limdi and Hyde, 2003; Gowda et al., 2009; Modaresi et al., 2011). Both AST and ALT are normally present in serum at low levels. Both AST and ALT are released into the blood in greater amounts when hepatocytes are damaged (Nyblom et al., 2004; Arag et al., 2010). HDL is one of the five significant groups of lipoproteins which allow lipids like cholesterol and triglycerides to be transported within the water-based blood flow. LDL also is one of the five significant groups of lipoproteins. Higher levels of LDL advance health problems and cardiovascular disease, they are often called the bad cholesterol (Adam et al., 2000; Barter et al., 2007).

Multiple plants and polyherbal formulations are used for the treatment of liver diseases. One plant may not have all the desired activities. A joining of different herbal extracts is to provide desired activities to treatment severe liver diseases (Hari kumar et al., 2011). So we decided to investigate the effects of extract from *Artemisia deserti* on the liver. Medicinal plants, since time ancient have been in use for treatment of diseases. In general, medicinal plants are the spine of the medicine (Zulfiker et al., 2010; Molan et al., 2012). The genus Artemisia is between the largest and most widely divided genera of the family Asteraceae (Erel et al., 2012).
Artemisia contains small herbs or bush found in northern temperate regions. Artemisia species grow in temperate weather conditions of both hemispheres, usually in dry or semiarid habitats. Thirty-four species of the Artemisia are found in Iran. The Artemisia has been inspected chemically in which acetylenic compounds, flavonoids, coumarins and terpenoids, specifically sesquiterpene lactones have been reported. This genus belongs to the useful aromatic and medicinal plants (Rustaiyan et al., 2000; Nahrevanian et al., 2010; Kazemi et al., 2011). The extracts of Artemisia plant have insecticidal, anti-parasitic, anti-fungal, sedative, anti-cough activity and it used for medicinal and ornamental and culinary(Wang et al., 2011). Also, in another study, 16 components were recognized in the oil of aerial parts from A. deserti, Camphor (45.5%), 1,8-cineole (16.7%), piperiton (8.6%), β-pinene (5.7%) and isoborneol (3.2%) were the major components in the oil of A. deserti. Thus the oil of A. deserti consists of 5 monoterpene hydrocarbons (8.4%), 9 oxygenated monoterpens (75.7%) and 2 sesquiterpenes (0.9%) (Kazemi et al., 2011).

Also, the leaf and flower oils of A. deserti were observed to be rich in oxygenated monoterpens (68.2% and 59.2% respectively) while oxygenated monoterpens (37.9%) and sesquiterpenes (33.8%) were the major in stem (Rustaiyan et al., 2000). The aim of this study was to evaluate the effect of extracts from Artemisia deserti on liver enzymes and tissue.

**MATERIAL AND METHODS**

**Collection of plants**

The flowering taps of A. deserti were collected in west of Esfahan area (Golpaygan heights), province of Esfahan, Iran, in September 2012. The voucher specimen was deposited at the herbarium of the Research-Institute of Esfahan Forests and Rangelands.

**Preparation of Extract**

The flowering taps of A. deserti were air-dried under shade and ground in to fine powder using electric blender, then, 20 gr of flower powder were extracted with 150 mL 80% ethanol by soxhlet extraction for 8 hours. The residue was evaporated by using a rotary evaporator. The dried extracts were stored at 4 °c until used. The extracts were dissolved in saline at the concentrations of 100, 200 mg/kg (Ene-ojo et al, 2013).

**Animals**

Adult male wistar rats (200-250 gr) were obtained from Iran Pastor Institute and divided into tree groups of eight animals each. They were maintained under controlled temperature, 12 h light/12 h dark conditions for 1 week before the start of the experiments for adaption to laboratory conditions. The procedures in this study were carried out in accordance with the institution’s scientific procedures for animals and was approved by the Institutional animal care and use committee. In the present study, a total of 24 rats were used. They were randomly divided in to the saline injection group (group1) and treatment groups. Thus, the treatment groups were induced by intraperitoneal injection of a freshly prepared solution of extract (100, 200 mg/kg body weight) in serum solution respectively daily for 6 days (group 2, 3) (Nahrevanian et al, 2010; Jayasimha et al, 2011). The animals were anesthetized and the blood samples were collected 2 days after the last injection. The biochemical parameters such as AST, ALT, ALP, HDL and LDL were assayed using autoanalyzer (902 Hitachi Automatic Analyzer, Roche, India). Then, the animals were dissected and liver tissue was fixed in 10% formalin, dehydrated in ethanol, cleared in xylene, and embedded in paraffin. Sections were prepared and then stained with Hematoxylin and Eosin (H&E) for photomicroscopic (Olympus, Japan) observation.

**Statistical analysis**

All data were presented as mean ± SEM. The statistical comparisons were done with analysis of variance (ANOVA) test by SPSS 18 software.

**RESULTS AND DISCUSSION**

No significant changes in liver parameters (AST, ALT, ALP, HDL, LDL) were observed in all three groups that probably show the extract of A. deserti had no effect on liver function. Although the rate of AST, ALP, ALT, LDL and HDL were changed between groups but these changes were not significant (Table).

Figure (a) showed histological structure of liver in group 1. The liver is divided in to hepatic lobules formed of radially arranged strands of hepatocytes that extend from the central vein to periphery of the lobe. The hepatocytes strands are separated from each other by blood sinusoids. Treating animals with extract showed
several histopathological alterations. In groups 2 and 3, the central veins, portal veins and sinusoidal spaces were filled with blood. Histological examination showed the necrosis of hepatocytes and degenerating of nuclei. Also, the kupffer cells were activated and signs of fatty degeneration were observed. The central vein wall was damaged. Neutrophils and lymphocytes infiltration was abundant around the portal vein and bile duct. Also, Figure (b-e) showed disarrangement the hepatocyte cords.

Table1. The effects of A. deserti extract on liver biochemical parameters (ANOVA)

<table>
<thead>
<tr>
<th>Groups</th>
<th>AST (U/L) Mean ± SD</th>
<th>ALT (U/L) Mean ± SD</th>
<th>ALP (U/L) Mean ± SD</th>
<th>HDL (mg/dl) Mean ± SD</th>
<th>LDL (mg/dl) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>162.37 ± 16.12</td>
<td>57 ± 12.68</td>
<td>447.12 ± 92.09</td>
<td>67.25 ± 8.18</td>
<td>4.75 ± 3.55</td>
</tr>
<tr>
<td>100 mg/kg</td>
<td>135.25 ± 12.54</td>
<td>55.87 ± 16.94</td>
<td>354.62 ± 94.32</td>
<td>65.87 ± 11.78</td>
<td>4.72 ± 3.91</td>
</tr>
<tr>
<td>200 mg/kg</td>
<td>146 ± 27.91</td>
<td>60.12 ± 10.62</td>
<td>418.12 ± 106.10</td>
<td>60.25 ± 9.25</td>
<td>4.97 ± 3.62</td>
</tr>
</tbody>
</table>

P > 0.05  P > 0.05  P > 0.05  P > 0.05  P > 0.05
F = 1.63  F = 2.51  F = 1.32  F = 1.40  F = 0.011
of rats. Whereas, this result was not similar to the results of Iriadam et al. (2006), they were reported that no significant histopathological changes were observed in liver after treatment by A. herba alba aerial parts extract. Also, Shuhua and Catto (1989) in studies on mice, no toxicity observed of artemisinin. This is probably due to the high content of flavonoids and antioxidant capacity. Another researcher no significant alterations were observed in the liver of the rats on the 2% A. abyssinica diet whereas reduction in cytoplasmic basophilia with small fatty vacuoles in the centrilobular hepatocytes were observed in all the rats on the 10% diet. This indicated the sensitivity of the animals to plant materials was dependent to the active ingredient and concentration added to the diet (Adam et al., 2000).

In another study that was similar to our results, the researchers were observed pathological changes in liver tissue, including inflammation and congestion, centrilobular necrosis, steatosis and swelling of hepatic cytoplasm with extract of A. dracunculus. These are possibly due to the presence of methylchavicol and other genotoxic compounds in the extract and this study was shown a direct correlation between extract dosage and three major variables: mutagenicity index, serum liver enzyme activity and liver histopathology (Kalantari et al., 2013).

In present study no significant changes in liver factors were observed with treatment of extract of Artemisia deserti. Whereas Iriadam et al. (2006) indicated that A. herba alba aerial parts aqueous extract caused reductions in ALT and AST. In the other hand, Adam et al. (2000) reported the rats fed a diet consisting of 10% A. abyssinica leaves extract the AST and ALT were higher than in the controls. The increase of these factors, indicative of liver damage. Another researcher were observed in treated animals with leaves essential oil of Artemisia annua, ALP was increased compared with the controls. This increase is probably due to involve this enzyme in the detoxification process and the reduction of ALP was shown in liver diseases (Amirmohammadi et al., 2012). This results were not similar to the our results.

Whereas in the other study no significant changes were observed in the serum ALT activities, however, the value of AST increased after 3 month oral administration of single dose (100 and 1000 mg/kg) of Artemisia afra aqueous extract. Also, suggesting that the AST activity levels increased with time, but ongoing treatment with high dose of aqueous extract removed this elevation, also, the extract may have a liver protecting effect. (Mukinda and Syce, 2007). Also, Soqeer (2011) conclude that the activity of AST was significantly reduced next management of A. monosperma extract in rat. This extract was increased antioxidant enzymes so for this reason, the rate of AST was reduced. Elsewhere, Kim et al. (2012) reported that levels of LDL decreased significantly with leaves powder of A. vulgaris L. in diets. On the other hand, the HDL levels significantly increased in broiler. This is probably due to the high content of flavonoids and antioxidant capacity (Kim et al., 2012). Jafari-Dinani et al. (2010) were observed that LDL in the A. aucheri group is decreased while HDL increased as compared to the high-cholesterol diet group (Jafari-Dinani et al., 2010).

Sesquiterpene lactones constitute a large group of biologically active plant chemicals that have been identified in several plant families such as Asteraceae. Artemisinin is a sesquiterpene lactone that existen in Artemisia genus (Chaturvedi, 2011). In vitro metabolic studies with human liver microsomes that had the ability of metabolizing different drugs showed that artemisinin was metabolized majorly by the CYP450 enzyme and CYP2B6 with a secondary contribution of CYP34A in individuals with low CYP2B6 expression. Ferreira et al. (2010) reported that bioavailability of artemisinin was reduced five-fold after five days of continuous oral administration, but p-glycoproteins were not involved in artemisinin release from the cells. They speculate that artemisinin will have a better if take for a short period because, after 5-7 days of treatment, pharmacological levels of artemisinin in the blood would decrease significantly due to degredation by induced CYP450 enzymes (Ferreira et al., 2010). Adam et al. (2000) reported the presence of alkaloids, flavonoids, sterols, tannins, volatile oils, and anthraquinones in aerial parts of the Artemisia species. These parameters were considered according to findings of Iriadam et al. (2006) for hepatotoxicity. Therefore, from our results we concluded that, no significant changes were observed in liver enzymes and LDL, HDL. Whereas, the flowering taps extract of A. deserti caused several histopathological alterations. These observations indicate minimal hepatotoxicity potential of A. deserti in rats. It also seems liver tissue disorders is resolved with time. So the further studies are needed in this context.
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REFERENCES


