GAVIN PUBLISHERS

Archives of Pediatrics

Modaresi M. Arch Pediatr 2: JPED-127.
DOI:10.29011/2575-825X.100027

Research Article

Effect of *Lavandula officinalis* Hydro Alcoholic Extract on Liver Enzymes and Histology

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Citation: Modaresi M (2017) Effect of *Lavandula officinalis* Hydro Alcoholic Extract on Liver Enzymes and Histology. Arch Pediatr 2: 127. DOI:10.29011/2575-825X.100027

Received Date: 19 August, 2017; **Accepted Date:** 04 October, 2017; **Published Date:** 12 October, 2017

Abstract

Liveris a vital organ in the body and has a key role in regulation of many physiological phenomena. Any disorder in liver operation causes a collection of physiological and anatomical disorders and kinds of different diseases. Considering consumption of the drug plants in traditional medicine. In this study 50 mature female mice were used with weight between 28-30 gr including 5 groups which each one has 10 mice. Study groups including control group without any drug treatment, placebo group only treated with normal saline solution every other day and three experimental groups that respectively have received 50,100 and 200 mg/kg doses of *Lavandula officinalis* hydro-alcoholic extract intraperitoneal. After 20 days, ALP, AST and ALT levels were measured and liver tissues of all groups were investigated by light microscope. The results were analyzed by SPSS software. ALT in comparison to control group increased significantly. AST enzyme in the maximum, moderate and minimum experimental groups respectively were 150.75±27.748, 147.38±42.051 that in comparison to control group showed significant decrease. Activity level of ALP enzyme in maximum dosage was 146.25±144.384 that in comparison to control group showed significant decrease. Observations indicated that the mice liver of 50and100 mg/kg treatment groups histologically had not pathological changes. But in dose 200mg/kg the liver tissue had pathologic changes as tissue necrosis that was indicator of liver serious damage, and thus indicated dose-related toxicity in dose 200 mg/kg. *Lavendula officinalis* hydro alcoholic extract decrease ceramic level of liver enzyme AST in dose 100 and 200 mg/kg and decrease serumic level of ALP in dose 200.But histological results indicate toxic and pathological effects on tissue. Thus, according to change effect of extract from dose 100 mg/kg to 200mg/kg and its toxic effect, effect of extract on liver is toxic.

Keywords: ALP; ALT; AST; *Lavandula officinalis*; Liver; Mice

Introduction

These days most of the plant drugs come into consumption market without doing any experiment. And public imagination is the drugs have not any toxicity. On the other hand, drug plants considering one of the important natural sources and were considered since much times ago and were used by human in traditional medicine for pain subsidence and drug plants have been used for curing many diseases. Among this plant is *Lavandula officinalis*, the plant from Lamiacea family, genus *Lavandula* [1,2].

Geographically its origin is desert and dry regions of Alps mountains and sandy soils of Mediterranean beach in south of France and Spain and also Toronto in Canada. The shrub and fragrant plant with height 1to 2 meters. The leaves are ever green. The French species blossoms in spring and English species blossoms in summer. Its stem is branching and covered with mutual narrow leaves.in end of stem has purple spike flower and has momentum fruit [3]. The part of plant that was used for remedy and extracting for perfume production is its flower that gives a green extract with bitter taste and pleasant odor [3]. It has antibacterial property. The most important constituents of extract respectively are: linalyl acetate and linalool (to60%), geraniol, coumarin, flavonoids, borneol, sterol, trapezoid, butyric acid, valeric acid [2,4]. Most of the past researches about this plant have focused on its effects on neurons and nervous system operation and positive effects in pain reduction، emotional stress، anti-anxiety and anti-depression effects [2, 5,6,7,8,9,10,11]. But there was a vacancy place of experimental research about its effects on liver. Liver is considered as a one of the vital organ in the body that has a key role in regulation of many physiological phenomena and any disorder

in its operation causes a collection of physiologic, anatomic and kinds of different diseases. Study of liver operation also have been considered by researchers [12,13]. Thus, considering that the side effects of *Lavandula officinalis* on liver biochemistry and histology wasn't considered until now. With considering that the enzymes are active in all body tissues such as liver [14], with measurement of ALT, AST and ALP serumic activity levels, cell damages could be discovered [15] in this study effects of *Lavandula officinalis* hydro alcoholic extract were evaluated and for this purpose the mature female mice Balb/C were studied for 20 days. Serumic activity levels of liver enzymes were measured in order to progress in knowledge of optimum use of this drug plant and determination of effective dose or doses. Also, the effects of this extract were studied on liver tissue to comparison enzyme results with histologic results to achieve conclusion.

Material & Methods

In this study 50 mature female mice Balb/C in weight range between 28-30 gr, were used that provided from laboratory animal section of Isfahan university of medical sciences**.** Animals were kept in 5 groups including 10 mices until time of experiment in standard cages and same condition with temperature range between 20-22 degree centigrade and light cycle12 hours lighting,12 hours' darkness. Sufficient water and food provided them and except in experiment time had access to food and water readily. And were experimented one time. In order to provide fresh flowers of *Lavandula officinalis* was referred to agricultural biotechnology institute of Iran's central region, located at NajafAbad-Isfahan road, and freshly harvested *Lavandula officinalis* were collected in order to obtain extract and were dried in far from sun light. Extraction and vaporizing to gain proper concentration, gained extraction was green and strong fragrance of lavender. 10 mice have died because of adaptation to new environment. And 40 mice have remained that divided into the 5 groups with 8 mice. Control group without any drug treatment, Placebo group which treated in 10 times regulatory every other day with normal saline and 3 experimental groups that respectively received intraperitoneal 50,100 and 200mg/kg doses of *Lavandula officinalis* hydro alcoholic extract and after 20 days (10 times, every other day) in head guillotine way, blood was taken. Gained blood samples were kept in laboratory condition for 20 minutes and were centrifuged for 15 minutes with 2000 rpm. After that serum of every tube has separated and transaminase enzymes were measured by auto analyzer apparatus. Data were analyzed with SPSS and Excel software's and t-student test. Significant difference between experimental and control groups considered with P value equal P≤0.05 (32) [16]. Mice livers were brought out by forceps and surgical knives carefully and after putting in the formalin 10%, tissue samples were ready for gaining slides and were cut with microtome apparatus and slides were studied histologically by light microscope carefully.

Results

Effect of *Lavandula officinalis* on liver enzymes according to gained results was as following: serumic amounts of ALT increased significantly (Figure 1).

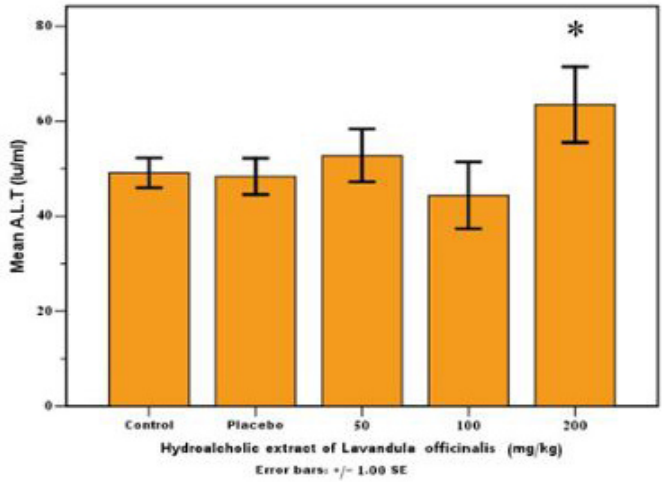

Figure 1: ALT enzyme ceramic levels comparison: comparison treatment groups to control and placebo.

In experimental groups ceramic amounts of AST enzyme with the increase dose from moderate to maximum respectively was (147.38±42.051), (150.75±27.748) that in comparison to control group (216.75±46.296) showed significant decrease (Figure 2).

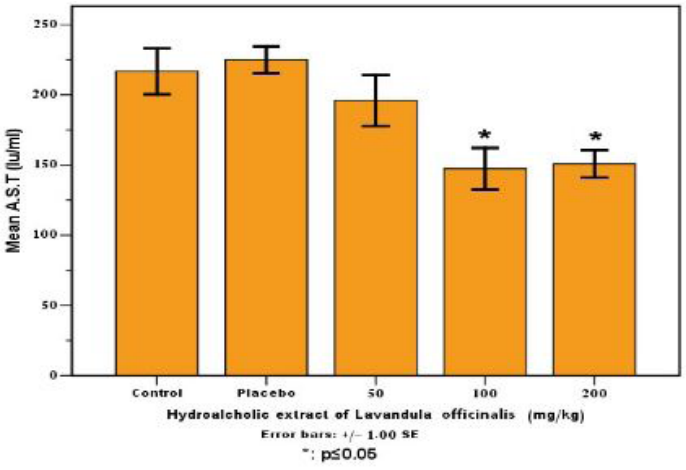

Figure 2: The comparison ceramic activity level of AST in *Lavandula officinalis* treatment doses with control and placebo group.

Also, ceramic activity levels of Alkaline Phosphatase (ALP) in experimental groups with increasing dose to maximum dose was 146.25±44.384 that in comparison to control group (216.63±49.367) showed a significant decrease (Figure 3).

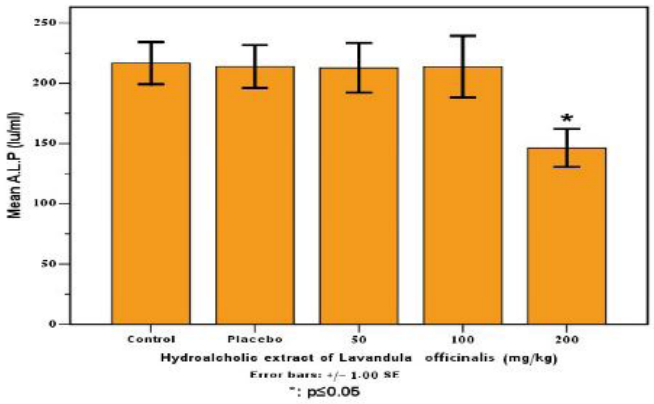

Figure 3: Comparison ceramic level of ALP activity in treatment groups in comparison to control and placebo groups.

Also, tissues became ready and obtained a thin layer with putting liver tissue in formalin 10% and doing all fixation stages and taking section. and finally, was studied by light microscope [12,16] in control group wasn't observed any pathological effect and liver tissue had completely normal view (Figure 4).

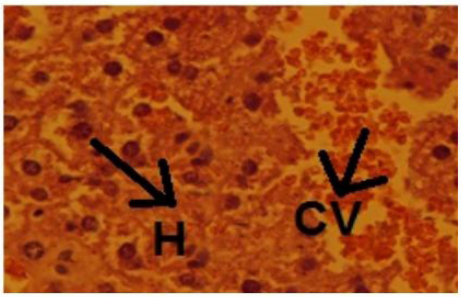

Figure 4: Microscopic Image of liver tissue in control group (zoom×400) (H: Hepatocytes) (CV: Central Veins).

Liver tissue of treatment group 50 mg/kg has a normal view and wasn't observed any significant pathological change (Figure 5).

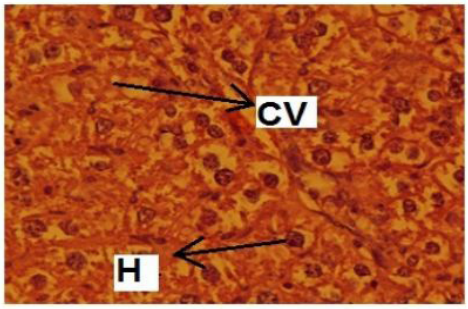

Figure 5: Microscopic image of liver tissue in treatment group dose 50 mg/kg(zoom: ×400) (H: Hepatocytes) (CV: Central Veins).

In liver tissue of treatment group 100 mg/kg, however the lobules have dense and hyperemia can be seen in central veins, but there is no view of phagocytic vacuoles and pathological effects and totally tissue has normal situation (Figure 6).

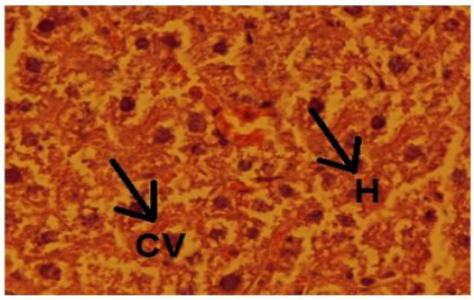

Figure 6: Microscopic Image of liver tissue in treatment group dose 100 mg/kg (zoom: ×400) (H: Hepatocytes) (CV: Central Veins).

But in tissue of treatment group dose 200 mg/kg there is much hyperemia in central veins. Basophilic nuclear accumulation can be seen that causes by destruction of liver cells. The tissue necrosis has made which is due to toxic effect of *Lavandula officinalis* extract of dose 200 mg/kg (Figure 7).

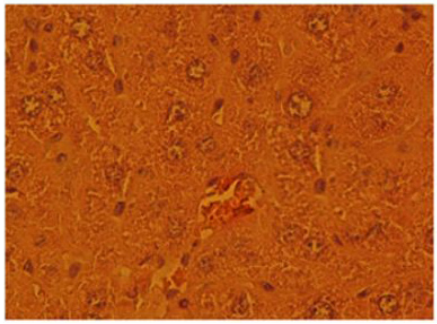

Figure 7: microscopic image of liver tissue in treatment group dose 200 mg/kg (zoom: ×400) (H: Hepatocytes) (CV: Central Veins).

Discussion

AST usually exists in different kinds of tissues such as liver, muscles, heart, kidney, brain. This enzyme inters to the blood stream when each one of these tissues were damaged. Ceramic level of this enzyme increases in liver parenchymal damage and heart and muscle damage. when the permeability of hepatocytes cell membrane is increased due to damage. This enzyme releases to blood stream furthermore [17,18]. Also, ALT naturally found in liver. This enzyme releases to blood stream because of liver damage. Thus, this enzyme somehow was used as a special marker of liver situation. Since the ALT is the most specific enzyme for liver damage [15]. Thus, considering results gained from this study, *Lavandula officinalis* hydro alcoholic extract has not any effect on ALT. alkali phosphatase predicated to those phosphatases which is active in 9-10.5 PH [19]. ALP ceramic activity level increases in pathological situation, bone losses and liver damages. Also increases in stop the flow of bile. In adults the enzyme in the serum has liver source. Measurement of ALP ceramic activity in liver,

bile and bone diseases is important [15,19]. Use of drug plants due to antioxidant activity and low side effects have been considered [20]. Plant sources can keep tissues safe from free radicals [20]. Linalyl acetate is an acetate ester of linalool. Linalool is terpene alcohol [21,22]. This compound is major compound in lavender [23]. According to past studies linalool and its derivatives have anti-inflammatory activity and flavonoids and geraniol that after acetate linalyl are major compounds in lavender [24] have proven its antioxidant activity in lamiae family including lavender [25-29]. Therefore, considering no increase of ceramic activity level of liver enzymes, it can be said that anti-inflammatory caused this response. In liver and hepatic diseases, the ceramic level of ALT and AST is increased. thus according to results which have gained, no change in ceramic activity level of ALT in treatment groups, and considering this enzyme is the most prominent liver enzyme that increases in liver damage[15], and considering with heart and liver damages, ceramic level of AST increases and with liver and bone damages ceramic level of ALP increases, Thus, can be concluded that no increase in ceramic level of AST and ALP indicates protective effect of the plant on liver, according to the newest studies use of those plants that including bioactive compounds has protective effect on tissue and biochemical activity of liver and causes decrease of Ceramic levels of liver enzymes such as AST and ALP[30]. and According to the significant reduction of ceramic activity level of AST in dose 100 and 200 mg/kg and significant reduction of ALP in dose 200 mg/kg and with considering that linalyl acetate and linalool (major compounds of extract) which is effective in reduction of stress and reduce activity of more than 100 genes which is effective in stressful condition[31] and also the anti-inflammatory activity of major compound(linalool and its acetate form [32], can be said this gained response totally causes decrease of oxidative stresses and facilitates anti-inflammatory responses and activates AMPK and PPAR-α pathway signals [30]. These factors cause decrease production of toxins and free radicals and finally decrease production of these enzymes [33]. But according to liver histological results that show plant extract has not pathological effect in doses 50 and 100 mg/kg. According to enzymatic results protective effect can be confirmed. But because of apparent pathological effect of dose 200 mg/kg on liver tissue that causes tissue necrosis and subsequently toxic effect on liver tissue, therefore can be considered that due to only with increase 100mg/kg dose of extract, emerging such a prominent, significant and destructive change on liver tissue, thus dose-related toxic effect is confirmed. According to Petti et al. study in 2012, activators of AMPK pathway and their activation, have anti cell proliferation role and it can cease cell proliferation in liver and according to results of Kladniew et al. in 2014 who verified linalool and its steer derivatives have anti cell proliferation and anti-cholesterol synthesis effect, and according to Petti article and comparison to Chang chie tang article that confirmed activation of AMPK and PPAR-αpathways have role in anti-inflammatory and liver protective reactions and also according to Lee et al. in 2013, the modulation of AMPK pathway has role in protection against liver damages(14) [34], it can be concluded that until a certain dose of *Lavandula officinalis* hydro alcoholic extract, the activation of the AMPK pathways signals causes anti-inflammatory activity and with increase dose, with Raff-MEK-ERK signaling, liver kinases of B1-AMP pathway, inhibits the active protein kinase LKB1-AMPK, which according to the Petti et al. study, causes inhibition of cell cycle and reduction of cell proliferation and causes liver tissue necrosis also according to Kladniew et al, inhibition of Mevalonate Pathway(MP) performs through inhibition of hydroxyl methyl glotaryl coA (HMGCR) enzyme activity that this process inhibits cell proliferation and probably cell activity and also inhibits cholesterol synthesis which it can be reason of tissue necrosis and result of this study [35-38].

Conclusion

Although *Lavandula officinalis* hydro alcoholic extract has protective effect in doses 100 and 200 mg/kg and causes reduction of AST and ALP enzymes activity levels, but according to histology results, with increase dose from 100 to 200 mg/kg, the liver tissue suffered the severe tissue necrosis thus, totally *Lavandula officinalis* hydro alcoholic extract has dose-related toxic effect and finally has toxic effect on liver.

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