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**THE EFFECT OF AQUEOUS EXTRACT OF
HARMALA SEEDS ON SOME BIOCHEMICAL AND
HISTOLOGICAL PARAMETERS OF THE LIVER IN
HAMSTERS**

Annotation: The study was conducted on 24 male hamsters, at the age 1,5 months, weight of 200-350 g, divided into four groups. the first group was left as a control. Over a period of 6 weeks, the aqueous extract of the Syrian Harmala seed was dosed, in three doses (50, 100, 200 mg / kg), for the experimental groups (G2, G3, (G4), respectively. The enzymatic and histological study of the liver showed effects that were proportionally proportional to the dose, so test results

The level of the enzymes ALT AST and ALP, of group (G2) that were given 50 mg / kg, approach and slightly higher than that of the control group (G1) which was $0.72 \pm 35.70 *$, $0.78 \pm 61.60 *$, $0.58 \pm * 56.70$, respectively. When greater changes were observed in the functions of liver of group (G3) animals exposed to the dose 100 mg / kg, it led to an increase in the level of its enzymes ALT, AST, ALP. reflected This is due to the apparent disruption in the characteristic radial structure of the liver cells, and the presence many degenerative foci of necrosis. while enzymatic changes in the liver function of the animals of group (G4) affected by the dose 200 mg / kg more severe and reached $0.69 \pm 119.71 *$, $1.11 \pm 331.18 *$, $1.10 \pm 198.13 *$, respectively, It was accompanied by more pronounced changes in the structure of the liver, and features of cell necrosis (pyknosis or absence of a nucleus) are evident.

Key Words: Harmala, liver, enzymes, ALP, AST, ALT, hamsters.

ВЛИЯНИЕ ВОДНОГО ЭКСТРАКТА СЕМЯН НАРМАЛА НА НЕКОТОРЫЕ БИОХИМИЧЕСКИЕ И ГИСТОЛОГИЧЕСКИЕ ПОКАЗАТЕЛИ ПЕЧЕНИ У ХОМЯКОВ

Аннотация: Исследование было проведено на 24 хомяках-самцах в возрасте полутора месяцев весом 200-350 г, разделенных на четыре группы. первая группа была оставлена в качестве контроля. В течение 6 недель водный экстракт семян сирийского хермеля дозировали в трех дозах (50, 100, 200 мг / кг) для экспериментальных групп (G2, G3, (G4), соответственно. гистологическое исследование печени показало эффекты, которые были пропорционально пропорциональны дозе, поэтому результаты теста Уровень ферментов ALT AST и ALP группы (G2), которым давали 50 мг / кг, приблизился и немного выше, чем у контроля группа (G1), которая составила $0,72 \pm 35,70$, $0,78 \pm 61,60$, $0,58 \pm 56,70$ соответственно. Когда наблюдались большие изменения в функциях печени

у группы (G3) животных, подвергшихся воздействию дозы 100 мг / кг, это привело к на повышение уровня его ферментов ALT, AST, ALP, что отразилось, это связано с явным нарушением характерной радиальной структуры клеток долек печени и наличие многих дегенеративных очагов некроза при ферментативных изменениях в функции печени животных группы (G4), подвергшихся воздействию дозы, были на 200 мг / кг более тяжелыми и достигли $0,69 \pm 119,71$, $1,11 \pm 331,18$, $1,10 \pm 198,13$ соответственно, что сопровождалось более выраженными изменениями в структуре печени, и признаки некроза клетки (пикноз или отсутствие ядра) очевидны.

Ключевые слова: Harmala, печень, ALP, ALT, AST, хомяки.

1. Introduction:

The liver may suffer from many injuries, and the importance of measuring the level of Transaminase ALT (AST, ALP) enzymes comes from the possibility of their diagnosis, even before symptoms of the disease appear [1,c.167].

The *Peganum harmala* is a Zygophyllaceae plant, is widespread in the Middle East and North Africa, Central Asia, America and Australia, which spontaneously grows in quarry and sandy areas, and severe environmental conditions [2,c.417]. The biological and medicinal activity of the Harmala plant occur because of alkaloids, especially the Indolicians , which include Harmaline, Harmane, Harmine, and Harmalol [3,c.199].Harmala seed alkaloids are widely used in herbal medication as an anesthetic and analgesic, treatment of asthma, colon cramps, jaundice [4,c.101] and as a laxative and diuretic [5,c.328], and sexual enhancement in males[6,c.56]. It is also used to reduce blood sugar and treat high blood pressure and Parkinson's disease [7,c.52], And as an anti-inflammatory or bacteriostatic [8,c.438]. Despite the great medicinal benefits of Harmala Seed, it has strong toxic effects, if consumed without caution as well [9,c.558], the lethal dose (LD50) in rats is 420 mg / kg. The results of studies [10,c.1] on the harmful effects of the alcoholic extract of Harmala (1000, 2000

and 3000 mg / kg) in the liver and kidney tissues of the white rats indicate a noted hyperemia, glomerular hypertrophy and inflammatory cellular infiltrations. The study indicated [11,c.68] the high level of hepatic enzymes ALP, SGOT, SGPT, due to the effect of the dose of 200 mg / kg of Harmala seed extract, and caused by the disturbance of liver and kidney functions and pathological changes that ranged between acute hepatitis and renal insufficiency. In view of the wide spread of the plant in our environment, and its widespread use in popular recipes, with the potential benefits and dangers, in addition to the recent research interested in the subject, and the lack of those interested in the Syrian Harmala on the hamster, our aim is to contribute to this study.

2. MATERIALS AND METHODS:

The study was conducted on hamsters, about 1,5 months old, weight of 200-350g, It was inhabited in laboratory conditions , 12-12 hour dark-light cycle, at temperature of 25 ± 3 , according to recommendations [12].

2.1. aqueous extract Preparation of the Harmala plant seeds: The extract was prepared by adding 50 g of Harmala Seed Powder, to 500 ml distilled water, then mixing for 15 minutes, after which was left for 24 hours and then filtered. To obtain the dry matter, we used a rotary evaporator, then preserved at a temperature of 4°C until Use [13,c.124].

2.2. Experiment Design:

The study was conducted over a 6-week period, using 24 hamsters, divided into four groups: 1- First (G1): a control group which animals drank water without additives.

2-The second (G2): which was given the extract in a dose of 50 mg / kg.

3-The third (G3): The extract was given in a dose of 100 mg / kg.

4-Fourth Group (G4): Harmala Seed Extract was given at a dose of 200 mg / kg. The end of the experiment was blood drawn to the biochemical tests, then euthanasia, animal dissection, and recording of histopathological changes.

2.3. Biochemical tests

The level of Aspartate amino Transferase (AST) or SGOT, and Alanine amino Transferase (ALT) or SGPT enzymes in the serum, was estimated according to [14,c.652], by the ready solutions prepared by the German company (Human), 340 nm. As for the Alkaline Phosphatase (ALP) level estimation, it was done according to [14,c.652] by the ready solutions prepared by the French company (BIOLABO), and the use of the photometer, at the absorption wavelength of 340 nm.

2.4. Histological study:

The tissue samples were fixed in 10% neutral formalin, the slides were prepared and dyed with hematoxylin-eosin (H&E) using the method [15,c.258], then studied under a microscope with x400 magnification.

2.5. Statistical analysis:

One way ANOVA test was used, using the SPSS statistical program. Mean and standard deviation were obtained and significance was calculated at the level of probability of significant difference compared to control group G1 ($P < 0.05$).

3. Results of the biochemical study:

The results shown in Table (1) of the effect of aqueous extract of Harmala's seeds on liver function showed a significant increase in the level of serum enzymes ALT, AST and ALP ($P < 0.05$) among the control groups compared with the control.

Table (1): The average level of Amino Transferase serum enzymes, in animal, the end of the experiment.

Arithmetic mean [X] and the standard deviation [SD] of (ALP)	Arithmetic mean [X] and the standard deviation [SD] of (AST)	Arithmetic mean [X] and the standard deviation [SD] of (ALT)	N	the group
0.58±*56.70	0.78 ±61.60 *	0.72 ±35.70*	6	Control
0.97±148.32*	0.84 ±115.91*	0.58 ±49.33*	6	50mg
0.69±*171.01	0.87 ±*205.16	0.97 ±94.17*	6	100mg
1.10±198.13*	1.11 ±331.18*	0.69 ±119.71*	6	200mg

3.1.The results of the histological study:

The hepatic tissue preparations of the second group animals (50 mg / kg) were almost identical to the control samples (Figure 1). except for the observation of cellular degeneration and the beginning of cellular necrosis (Pyknosis in some nuclei corresponding to a nuclear duplication in Some cells) and foci of inflammatory cell assembly around the vein in other sections (Figure 2)

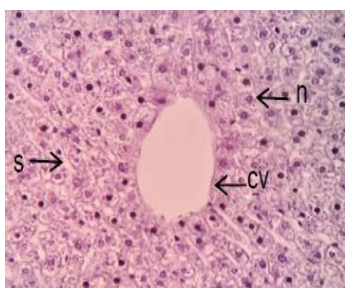


Figure 1: Histological section of Liver the control (H&E x400)

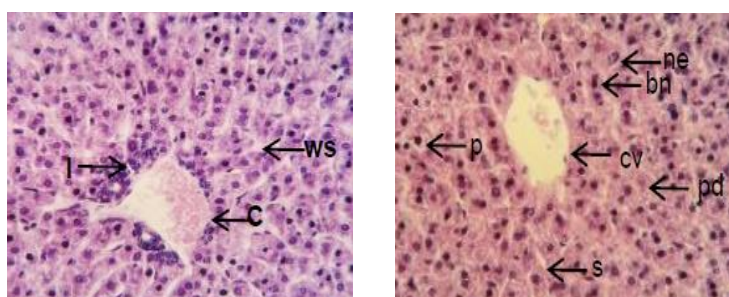


Figure 2: Histological section of Liver the the group G2 (H&E x400)

As for the liver samples of the third group animals (100 mg / kg), they show congestion and damage to the blood vessel walls, instances of cloudy swelling in the liver cells, enlargement of their nuclei, disruption and expansion of hepatic sinuses, inflammatory cellular infiltration and fatty degeneration in the cytoplasm of hepatocytes, Figure (3)

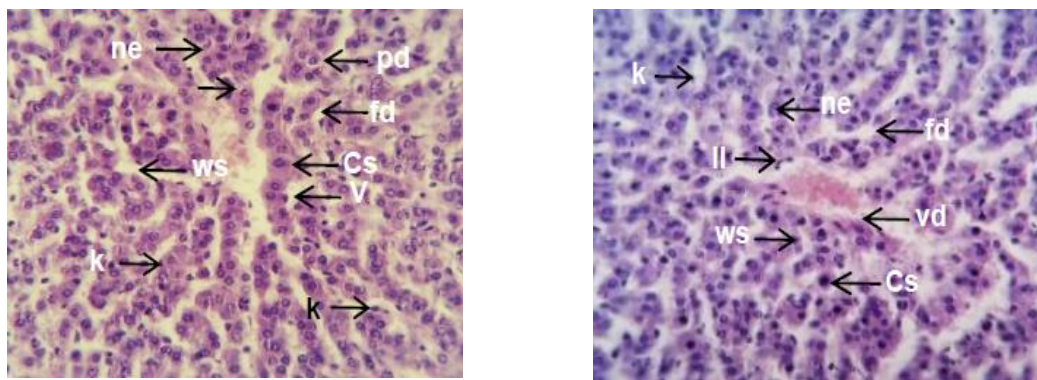


Figure 3: Histological section of Liver the group G3(H&E x400)

As for the liver samples of the fourth group exposed to the dose of 200 with / kg, the most severe changes were in the form of cell swelling, aqueous degeneration and hepatic cellular lesions, with a lipid degeneration and lobular cell necrosis observed (Figure 4).

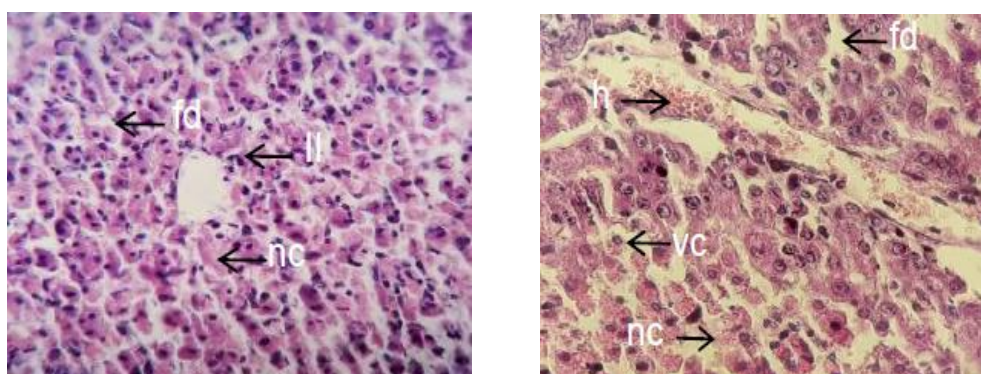


Figure 4: Histological section of Liver the group G4(H&E x400)

4. Discussion

The current study showed that the chronic effect of aqueous extract of Harmala seed, had resulted in liver function disorder, and the high level of its enzymes ALT , AST and ALP compared to the control group, and confirmed by histological changes with the effect of doses 100 and 200 mg / kg after, which

were summarized by cloudy swelling and the beginning of fatty degeneration. In the cells of the lobules, focal necrosis, and inflammatory infiltration, Consistent with the results [11,c.68] in terms of liver function disorder, the high level of amine transporter enzymes. and what [10,c.1] mentioned about hepatic cell necrosis, vacuolization and Pyknosis. In addition to circulatory disorders, and inflammatory infiltration. It also agrees with what has been confirmed by [16,c.30] that the seed extract of Harmala has been raised to the level of ALT and AST enzymes, compared to the control group.

However, the results of this study are inconsistent with its findings [17,c.1] by giving the alcoholic extract of Harmel seeds at a concentration of 200 and 300 mg / liter for chicken with drinking water..

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