

¹Magbolah Salem
Helal Alzahrani

Therapeutic Functions of Artemisia Judaica in Rats Injected with Carbon Tetrachloride (Ccl4)



Abstract: - There are many types of liver disease, which can be caused by infections, inherited conditions, obesity and misuse of alcohol. Over time, liver disease may lead to scarring and more serious complications, so we worked on this investigation to magnify the therapeutic applications of Artemisia judaica in carbon tetrachloride-injected rats (Ccl4). The experiment was carried out in a caged animal. All rats were fed a basal diet for one week before the study, and they were divided into five groups, each with six rats. As control negative normal rats (C-ve), the first group sample was fed only the basal diet for 28 days. The remaining rats (n=24) were injected with carbon tetrachloride (Ccl4). Four groups were fed varying concentrations of (5%, 10%, 15% Artemisia judaica, whereas one group was diagnosed with the illness and disease, and didn't even feed the experimental diet. The results showed that highest value of feed efficiency ratio (FER) was found in 15% Artemisia judaica. It is noticed that a significant decreases in BWG% for the control group compared to all groups. Also, The strongest effect in serum AST levels was recorded for group 5 which fed on 15% Artemisia judaica, while the rats fed on different levels of Artemisia judaica were lower than the positive control group and higher than the negative control groups. The study recommended feeding Artemisia judaica in different concentrations, especially 15%.

Keywords: Artemisia judaica, Therapeutic functions, carbon tetrachloride, hepatocellular.

I. INTRODUCTION

Artemisia judaica is considered one of the herbs with a strong and fragrant smell. It has been called by many names. The herb is available in places where there are valleys and plains in the Mediterranean Red Sea. All parts of the herb are used because they contain many excellent unstable essential oils and some pungent substances, and they are known as wild herbs [1]. It is known as an immortal plant and has leaves that remain for many years. The plant is one to one and a half meters long, with a woody stem and an excellent red color [2, 3]. In addition to the presence of the petiole leaves on which the yellow cluster leaves grow, It has very fine roots with a strong but unpopular scent, [4] *Artemisia judaica* L. (Arabic name: Beithran), is a medicinal and aromatic plant growing in the valley bottoms of desert areas, particularly in the southern desert of Saudi Arabia borders [5, 6]. It is used for the treatment of stomach ache, heart diseases, sexual weakness, diabetes, gastro-intestinal disorders and external wounding. Additionally, other folk medicines of the Arabic region commonly use this aromatic plant for the treatment of inflammatory-related diseases, for instance fungal infections, diabetes, atherosclerosis, cancer and arthritis [7]. *Artemisia judaica* (ArJ) is a Mediterranean aromatic plant used traditionally to treat gastrointestinal ailments, skin diseases, atherosclerosis, and as an immuno-stimulant. This study describes ArJ essential oil constituents and investigates their wound healing activity [8]. *Artemisia absinthium* is claimed to possess [antifungal](#), [neuroprotective](#), [insecticidal](#), [antimicrobial](#), [anthelmintic](#), [acaricidal](#), [antimalarial](#), [antidepressant](#), and [hepatoprotective](#) properties. It is an ingredient in the spirit [absinthe](#), and is used for flavouring in some other [spirits](#) and [wines](#), including [bitters](#), [bäsk](#), [vermouth](#), and [pelinkovac](#). As medicine, it is used for [dyspepsia](#), as a bitter to counteract poor appetite, for various infectious diseases, [Crohn's disease](#), and [IgA nephropathy](#) [9].

The liver has many important functions, including digesting your food and processing and distributing nutrients. There are many kinds of liver diseases and conditions. Some, like hepatitis, are caused by viruses. Others can be the result of drugs or drinking too much alcohol. Long-lasting injury or scar tissue in the liver can cause cirrhosis. **National Institute of Diabetes and Digestive and Kidney Diseases(2021)** [10]. It turns nutrients into chemicals your body needs. It filters out poisons. It helps turn food into energy. So when your [liver](#) doesn't work well, that can affect your whole body. **The Lecturio Medical Concept Library(2021)** [11].

II. AIM OF STUDY

Investigate the therapeutic functions of *Artemisia judaica* in rats injected with carbon tetrachloride (Ccl4).

III. Materials and methods

Materials

Preparation of Artemisia judaica: *Artemisia judaica* are properly cleaned, cut into small slices, and dried for 3- days at 50 °C in a drying oven, before crushing and grinding into a powder form.

¹ Biology Department, Faculty of Science, AL-Baha University, Saudi Arabia

Experiential animals: In this investigation, 30 male albino rats of the Sprague Dawley breed weighing 150 ± 10 g were used.

Biological experiment

Rats' normal diet:

The basil diet contained 10% casein, 0.25% choline chloride, vitamin mixture (1%), 5% cellulose, 10% maize oil, 4% salt mixture, 0.35% methionine, and corn starch (69.5%) [12].

The basal diet in the test contained CaCO_3 (600 mg), $\text{MgSO}_4 \cdot 2\text{H}_2\text{O}$ (204 mg), K_2HPO_4 (645 mg), $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (150 mg), $\text{Fe}(\text{C}_6\text{H}_5\text{O}_7) \cdot 26\text{H}_2\text{O}$ (55 mg), ZnCl_2 (0.5 mg), $\text{MnSO}_4 \cdot 4\text{H}_2\text{O}$ (10 mg), NaCl (334 mg), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.06 mg) and K_1 (1.6 mg), [13].

The basal diet in the test contained Vitamin A (200 Iu), Vitamin K (0.50 Iu), Vitamin E (10 Iu), Calcium pantothenic acid (0.40 mg), Thiamin (0.50 mg), Pyridoxine (1.00mg), Vitamin D (100 Iu), Folic acid (0.02 mg), Niacin (4.00 mg), Para-amino – benzoic acid (0.02 mg), Choline chloride (200 mg), Inositol (24 mg), Vitamin B12 (2.00 g) [14].

Diet experiment

Table 1 shows the experimental diet, which is made up of the basic diet with powdered plants supplemented at a 10% rate.

Table (1): The basic and experimental diets' compositions.

Component (g)	Basal diet	5% <i>Artemisia judaica</i>	10% <i>Artemisia judaica</i>	15% <i>Artemisia judaica</i>
Test ingredients	---	5	10	15
Casein	20	20	20	20
Corn oil	4.7	4.7	4.7	4.7
Mineral mix	3.5	3.5	3.5	3.5
Vitamin mix	1	1	1	1
Cellulose	5	5	5	5
Cholin chloride	2	2	2	2
Sucrose	10	10	10	10
Corn starch	Up to 100	Up to 100	Up to 100	Up to 100

Carbon tetrachloride (Ccl_4).

El-Gomhoria Company for Chemical Industries in Cairo, Egypt, provided the compound (Ccl_4) carbon tetrachloride in a 10% liquid solution. It was distributed in white plastic water bottles holding one litre as a toxic substance ingredient for liver disease, according to **Passmore and Eastwood (1986)** [15]. It is diluted using paraffin oil obtained from the drugstore during the induction.

Rats

mature male Sprague-Dawley albino rats, weighing (B.Wt)150-160 g. At the age of 14-16 weeks, the animals were transferred from the Animal Laboratory. The animals were kept in plastic cages with stainless steel covers and were kept in very clean conditions. For adaption, rats were given the basal diet for Seven days prior to the study. A smallmouth bottle connected with a metallic tube and a piece of plastic tubing at the mouth provided Ad libitum water. As previously indicated, rats were acclimatized on a 12-hour light/12-hour night condition for seven days prior to the beginning of the research to allow for acclimation.

Induction of liver intoxication in rats

Jayasekhar, et al., (1997) used intramuscular injections of (Ccl_4) carbon tetrachloride into paraffin oil 50% V/V (2ml/kg B.W.T.) twice per week for two weeks to induce chronic liver injury in male albino rats [16]. Following Ccl_4 injection, blood samples were obtained via the retro-orbital technique to confirm the presence of liver injury and to test liver function.

Animal Groups and Experimental Design:

- Each group of six rats was divided into seven groups. The following were the rat groups:

- G₁: Normal rats fed a basic diet for 28 days without any treatment as the positive control (Control group).
- • G₂: Rats with liver toxicity were kept as control negative and fed a basal diet for 28 days without any treatment.
- G₃: Rats with liver intoxication and fed on basal diet plus 5% of *Artemisia judaica*.
- G₄: Rats with liver intoxication and fed on basal diet plus 10% of *Artemisia judaica*.
- G₅: Rats with liver intoxication and fed on basal diet plus 15% of *Artemisia judaica*.

Biological evaluation:

Each day for the 28-day study, the amount of food consumed was noted, and body weight was recorded each week. The feeding efficiency ratio (F.E.R.), the body weight growth (B.W.G. %), and the organ weight were all calculated [17].

Blood sampling:

At the end of this study, blood samples were obtained following a 12-hour fast. The retro-orbital approach with highly specialized glass tubes was used to collect blood samples into a dry clean centrifuge tube and let them to coagulate for half an hour in a water bath (37 °C) at room temperature. Before testing for glucose, blood samples have been centrifuged for 10 minutes at 3000 rpm to extract the serum. The residue was carefully aspirated, put into clean, tight-fitting polypropylene tubes, and maintained frozen until analysis at (-20 °C).

The liver, kidney, heart, and spleen were extracted and washed in salt solution before being weighed and preserved in 10% formalin, as specified by **Drury and Wallington(1980)**.

Biological evaluation:

Feed efficiency ratio (FER), food consumption, body weight gain % (BWG%), and FER (feed efficiency ratio). Using the equation following [17]:

$$\text{Using the equation below. } BWG\% = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

$$FER = \frac{\text{Gain in body weight (g / day)}}{\text{Food Intake (g / day)}}$$

$$\text{The relative weight of organs} = \frac{\text{Organ's weight}}{\text{Animal body weight}} \times 100$$

Analytical biochemistry:

Measurement of liver enzyme activity

Measurement of aspartate aminotransferase (AST) activity:

The AST enzyme was determined using a spectrophotometer and particular kits (BioMerieux) in accordance with **Reitman and Frankel (1957)** [18].

. Measurement of serum alanine aminotransferase (ALT) activity:

The calorimetric technique described was used to test the activity of the ALT enzyme [18].

Estimation of serum total cholesterol: In accordance with **Ratliff and Hall (1973)** [19], the total cholesterol level was evaluated.

Triglyceride measurement: According to **Jacobs and Van Denmark (1960)** [20], the enzymatic colorimetric assessment of triglycerides has been established .

Estimation of HDL: Following Jacobs and **Van Denmark's standards, HDL was tested (1960)** [20].

Determination of VLDL and LDL: The following procedure was used to determine VLDL and LDL using Lee and Nieman's (1996) method [21].

Statistical analysis

A one-way categorization was used to calculate the statistical analysis. According to the least significant difference (LSD) and analysis of variance (ANOVA) (LSD) [22].

IV. RESULTS AND DISCUSSION

The main goal of this study to evaluate the therapeutic functions of *Artemisia judaica* in rats injected with carbon tetrachloride (CCl₄).

Biological changes:

Data presented in Table (2) showed the effect of different levels of *Artemisia judaica* on body weight gain (BWG)(g), the feed efficiency ratio (FER), and feed intake (FI)(g/d) of hepatopathy rats.

It could be noticed in table (2) that differences between all mean values of these groups were significant when compared to control negative group. There are no significant differences in BWG among group 3 and 4. The best result was group 5 which fed on 15% *Artemisia judaica*.

Data present in Table (2) showed the effect of different levels of *Artemisia judaica* on feed intake (FI) and feed efficiency ratio (FER) (mean± SD).

Also data present in Table (2) showed that no significant differences in feed intake (FI) between positive controls and group 3. From the Table, it could be noted that the differences in values of feed intake between all treated groups were considerable as compared to negative and positive control groups. The obtained data revealed a high variation in feed intake between treatments and the controls group.

According to data present in the same Table (2), these results denote that there were significant increases in feed efficiency ratio (FER) for all groups when compared with control positive group. The highest value of feed efficiency ratio (FER) was found in 15% *Artemisia judaica*. It is noticed that a significant decreases in BWG% for control group compared to all groups.

From the obtained results, it could be observed that treating rats with the tested *Artemisia judaica* led to increase in BWG%, FI and FER when compared with both positive controls while lower than negative control. These results were in agreement with those reported by Calliste et al., (2001) who said that dietary fiber (DF) derived from *Artemisia judaica* have a relatively high proportion of SDF [23].

Table (2) showed the effect of different levels of *Artemisia judaica* on body weight gain (BWG)(g), the feed efficiency ratio (FER), and feed intake (FI)(g/d) of hepatopathy rats

Means in the same column with different litters are significantly different (P <0.05).

Groups	Parameters		
	B. W. G. (g)	F. I. (g)	F. E. R.
Control (-)	43.64 ^a ±4.21	11.71 ^a ±0.22	0.133±0.001
Control (+)	4.61 ^d ±0.13	2.63 ^d ± 0.11	0.063 ^d ±0.001
5% <i>Artemisia Judaica</i>	9.12 ^c ± 1.19	2.89 ^d ±0.02	0.112 ^b ± 0.001
10% <i>Artemisia Judaica</i>	12.74 ^c ± 0.21	4.76 ^c ±0.12	0.096 ^b ± 0.002
15% <i>Artemisia Judaica</i>	17.54 ^b ± 1.11	7.68 ^b ±0.27	0.082 ^c ±0.002

Data presented in Table (3) showed the effect of different levels of *Artemisia judaica* on liver functions (ALT, AST) of hepatopathy rats.

It could be observed Table (3) that in control negative group AST was 39± 3.00 u/l which significantly decreased when compared with positive control group. But, the levels of AST in groups 3, 4 and 5 showed significant increasing as compared to control negative group and significant decreased as compared to control positive groups. The strongest effect in serum AST levels recorded for group 5 which fed on 15% *Artemisia Judaica*

It is clear that the serum level of (ALT) in group 5 which fed on 15 % *Artemisia judaica* was the lowest level which being 77 ± 3.8 U/L and showing no significant change with group which fed 10% *Artemisia judaica* which was 82 ± 0.34 U/L. At the same time, rats which fed on 5% *Artemisia judaica* and positive control group significantly didn't differ in serum level of ALT [24]. Based on the chromatographic examination of the AME of A. Judaica, it was found that it was rich in flavonoids specially flavone type mainly apigenin and luteolin. Secondary metabolites identified from plants as flavonoids represent effective therapeutic agents for the treatment of various diseases like hepatosis, tumour suppressive and immune.

Table (3) showed the effect of different levels of *Artemisia judaica* on liver functions (ALT, AST) of hepatopathy rats.

Groups	Parameters	
	AST(U/L)	ALT(U/L)
Control (-)	$39^c \pm 3.00$	$45^c \pm 0.6$
Control (+)	$109^a \pm 3.21$	$95^a \pm 2.3$
5% <i>Artemisia Judaica</i>	$102^a \pm 5.01$	$90^a \pm 5.4$
10% <i>Artemisia Judaica</i>	$94^b \pm 5.34$	$82.66^b \pm 0.34$
15% <i>Artemisia Judaica</i>	$88^c \pm 7.76$	$77^b \pm 3.8$

Values denote arithmetic + Standard deviation of the mean. Means with different letters (a,b,c,d,e,f,g) in the same column differ significantly at $P < 0.05$, while those with similar letters are non-significant by different.

Data given in Table (4) showed the effect of different levels of *Artemisia judaica* on kidney function of hepatopathy rats .

It could be observed that the highest value of serum urea levels was found in rats found in positive control group . No significant changes were found in serum urea levels between groups 2 and 3 also, there is no significant between group 4 and 5.

It is clear that in control negative group creatinine levels was 0.46 ± 0.02 mg/dl which significantly decreased when compared with rats which found in positive control and group fed 5% *Artemisia judaica* . while, rats of groups 4 and 5, creatinine levels of these groups were no significant between each other and showed significantly increasing as compared to control negative group .Groups 5 was the lowest creatinine value which showing a significant decreased as compared to the other groups and a significant increased when compared with control negative group.

Gadah et al., (2020), designed to illustrate the protective effect of oral administration of *Artemisia judaica* extract (AjE) against hepatorenal damage in a high-fat diet/streptozotocin (HFD/STZ) rat model of hyperlipidemia and hyperglycemia [25]. Significant elevations in hepatic (AST and ALT) and renal (urea, uric acid, and creatinine) function markers were observed in the serum of diabetic rats. Additionally, STZ injection caused remarkable elevations in lipid peroxidation and nitric oxide levels as well as suppression of antioxidant markers (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione). Marked elevations in TNF- α and Bax levels with a decline in Bcl-2 levels were detected after STZ injection. Furthermore, TGF- β 1 expression levels were significantly upregulated in the liver and kidney tissues. Rats that received AjE or MET showed significant improvement in most of the aforementioned parameters, and the protective efficacy was higher for AjE than for MET. Histopathological screening confirmed the biochemical findings. Conclusively, our results illustrated the antihyperglycemic, antihyperlipidemic, antioxidant, anti-inflammatory, and antiapoptotic activities of AjE against hepatorenal injury in HFD/STZ-induced diabetes.

Table (4) showed the effect of different levels of *Artemisia judaica* on liver functions (ALT, AST) of hepatopathy rats.

Groups	Parameters	
	Urea (mg/dl)	Creatinine(mg/dl)
Control (-)	27 ^c ± 4.23	0.46±0.12 ^c
Control (+)	50.33 ^a ± 3.21	2.45±0.22 ^a
5% <i>Artemisia Judaica</i>	48.33 ^a ± 3.31	2.05 ±0.15 ^{ac}
10% <i>Artemisia Judaica</i>	43.33 ^b ± 4.12	1.53±0.35 ^b
15% <i>Artemisia Judaica</i>	40.3 ^b ± 1.1	1.35±0.50 ^b

Values denote arithmetic + Standard deviation of the mean. Means with different letters (a,b,c,d,e,f,g) in the same column differ significantly at P<0.05, while those with similar letters are non-significant by different.

Data given in Table (5) showed the effect of different levels of *Artemisia judaica* on lipid profile of hepatopathy rats.

In table (5) it could be noticed that the cholesterol of negative control was 87.2±26 while the positive controls were 265.2±2.7 The obtained results showed significant decrease in serum levels of total cholesterol in group fed on different levels of *Artemisia judaica* when compared with positive control groups. There were significant among the results of groups.

Data presented in table (5) revealed that control positive, the mean value of serum triglycerides was 195.8±0.83 mg /dl as compared to normal rats which was 56.47±0.15 mg /dl. Also, the results showed significant increase in serum of triglycerides in positive control groups as compared to control negative group. There were significant among the results of all groups.

Also table (5) obvious that control positive, the mean value of serum levels HDL-C was 30.81±1.15, mg/dl while normal rats the mean value of serum HDLC was 53.94±0.12 mg/dl. This is finding denote that there was significant decrease in control positive as compared to normal rats.

The value of serum levels HDL-C of groups fed on different levels of *Artemisia judaica* were lower than that of negative control group and higher than positive control group.

Data in table (5) showed the effect of different levels of *Artemisia judaica* on serum levels of low density lipoprotein cholesterol (LDL-C) .It could be noticed that the data evidence that, (LDL-C) levels was significantly elevated in positive control, the values were 89.9±4.14 mg/dl while for negative control group was 20.2±0.33 mg/dl.

It noticed in table (5), these results of LDL- c higher in positive control groups than normal rats, the rats fed on different levels of *Artemisia judaica* were lower than positive control group and higher than the negative control groups.

Salwa et al., (2009), indicated that, toxicological and pharmacological studies were carried out on the water and alcoholic extracts of *Artemisia judaica* (A. judaica) plant which is commonly used in folk medicine in Egypt [26]. Results obtained revealed that no mortalities in mice following oral administration of aqueous extract of A .judaica up 50 to 5g/kg, while in the alcoholic extract the LD was 9.17g/kg. Single and multiple doses (0.25 and 0.5 g/kg b.wt.) for the water extract, (0.5 and 1 g/kg b.wt.) for the alcoholic extract produced insignificant effect on serum cholesterol levels but there was significant decrease in serum triglycerides levels.

Table (5) showed the effect of different levels of *Artemisia judaica* on lipid profile of hepatopathy rats.

Groups	Parameters			
	Total Cholesterol (mg/dl)	Triglycerid (mg/dl)	HDL Cholesterol (mg/dl)	LDL Cholesterol (mg/dl)
Control (-)	87.2 ±2.6 ^d	56.47±0.15 ^e	53.94 ±0.12 ^a	20.2 ±0.33 ^e
Control (+)	265.2±2.7 ^a	195.8±0.83 ^a	30.81 ±1.15 ^c	89.9 ±4.14 ^a
5% <i>Artemisia Judaica</i>	192.9±1.81 ^b	176.6±3.63 ^b	31.12 ±1.78 ^c	75.6 ±0.19 ^b
10% <i>Artemisia Judaica</i>	175.7±1.71 ^c	169.9±1.65 ^c	36.13 ±2.07 ^b	63.7 ±1.34 ^c
15% <i>Artemisia Judaica</i>	147.1±3.04 ^d	158.3±1.55 ^d	39.7 ±0.13 ^b	54.9 ±0.66 ^d
Values denote arithmetic + Standard deviation of the mean. Means with different letters (a,b,c,d,e,f,g) in the same column differ significantly at P<0.05, while those with similar letters are non-significant by different.				

Data given in Table (6) showed the effect of different levels of *Artemisia judaica* on blood glucose of hepatopathy rats.

Data in Table (6) presented the effect of different levels of *Artemisia judaica* on blood glucose of hepatopathy rats.

The results in Table (5) indicated that the mean value of blood glucose for control positive 195.6±3.11 mg/dl, while the negative control group was 90.5±0.87 mg/dl. There was significant decrease in all groups as compared positive control group and significant increase in all groups as compared to negative control group.. The best group in glucose blood level was rats group fed on 15% *Artemisia judaica*.

Salwa et al., (2009) indicated that, toxicological and pharmacological studies were carried out on the water and alcoholic extracts of *Artemisia judaica* (*A. judaica*) plant which is commonly used in folk medicine in Egypt [26]. Results obtained revealed that no mortalities in mice following oral administration of aqueous extract of *A. judaica* up 50 to 5g/kg, while in the alcoholic extract the LD was 9.17g/kg. Single and multiple doses (0.25 and 0.5 g/kg b.wt.). The single and multiple doses of both water and alcoholic extracts significantly reduced the blood glucose level in experimentally diabetic rats while no significant effect was shown on normal rats.

Table (6) showed the effect of different levels of *Artemisia judaica* on blood glucose of hepatopathy rats.

Groups	Parameters
	Glucose (mg/dl)
Control (-)	90.5 ±0.87d
Control (+)	195.6 ±3.1 l ^a
5% <i>Artemisia Judaica</i>	176.1 ±2.1 l ^b
10% <i>Artemisia Judaica</i>	150.3 ±1.11c
15% <i>Artemisia Judaica</i>	135.3 ±1.15 c
Values denote arithmetic + Standard deviation of the mean. Means with different letters (a,b,c,d,e,f,g) in the same column differ significantly at P<0.05, while those with similar letters are non-significant by different.	

V. RECOMMENDATIONS

1. For hepatic patients, different levels of *Artemisia judaica* are recommended.
2. *Artemisia judaica* in different concentrations, especially 15% *Artemisia judaica*, can treat diabetes.
3. Different *Artemisia judaica* concentrations can be recommended for atherogenic index levels and decreasing LDL.

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