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# Effect of Doum (*Hyphaene Thebaica*) Fruit Water Extract on hypercholesteremic Rats

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**Abstract:** Background: (*Hyphaene thebaica)* Doum water extract (DWE) contained important active compounds, such as phenolic and flavonoids that work as an antioxidant which help to control hyperlipidemic. Aims: The study aims to compare between the effect of DWE and (Statins) hypercholesterolemia medication on hypercholesterolemic rats after 4 weeks of treatment. Methods: Fifty-six male albino rats (160 – 180 g) were divided into 7 groups, each group consisted 8 rats. Group (1) Control negative, Group (2) were Control positive groups which fed with high cholesterol diet (HCD), Groups (3) to (7) fed HCD and treat w/wo (Atorvastatin) at (40 mg / kg of body weight) and doum water extract at doses of (20, 40mg/kg b. wt). Body weight gain% (BWG %), relative weight of liver, serum levels of total cholesterol (TC), triglycerides (TG), lipoproteins fraction, and histopathological examination of liver were studied. Results: The results showed that, BWG% for hypercholesterolemic rat fed with DWE at two dosages (20, 40 mg/ kg) for four weeks was increased compared to control positive group. DWE significantly ($p<0.05$) decrease total cholesterol, triglycerides and LDL concentrations compare to control positive group. Values of HDL concentration were significantly increased in all treated groups compared to control positive group. As well as a significant ($p<0.05$) reduction of liver weight at two dosages (20, 40 mg/ kg) by (14.79%) and (7.30%) respectively, than to control positive group. Histopathological analysis of liver section of rats that treated with DWE showed amelioration improvement of histological changes caused by high level of cholesterol when compared with control positive group. Conclusion: The study clearly revealed that consumption of DWE showed improvement of health status. Human studies are needed to confirm that effect on hypercholesterolemia.
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**Key words:** Doum *Hyphaene thebaica*, rats' hypercholesterolemia, body weight gain% (BWG %), High Cholesterol Diet (HCD).

## 1. Introduction

Doum (*Hyphaene thebaica)* fruit define as an edible fruit with oval shape comes from a desert palm tree. The doum palm naturally found in northern half of Africa and Arabian Peninsula **(Vandenbeldt, 1992).** The mesocarp in some palm is very aromatic and sweet with a taste like ginger bread. Doum fruit has been used as an anti-hyperlipidemia drug **(Sa'adah *et al.*, 2017).** According to **Bayad (2016)** the fruits of *H. thebaica* have antimicrobial, antioxidant, antidiabetic, antihypertensive and hypolipidemic effects.

Doum has nutritional and pharmacologic properties **(Aboshora *et al.* 2014).** It contained high amount of amino acids valine, leucine, and some non-essential amino acids such as (alanine, aspartic acid, glutamic acid, glycine, serine and proline). Also it was very rich in minerals such as potassium (K) and phosphorous (P) **(Abdel-Rahman 2011).**

In addition, the phytochemical components which found in doum extract are classified as antioxidants such as phenolic compounds, flavonoids, tannins and saponins. Antioxidants due to their capacity to donate hydrogen atoms may encourage browning of white adipocytes, elevate energy consumption, prevent high-fat diet (HFD)-encouraged obesity and become a better metabolic situation. Elevating the activity of brown adipose tissue (BAT) and encouraging white adipose tissue (WAT) browning are promising means to elevate energy consumption and get better glucose and lipid metabolism. Flavonoids inhibit lipid oxidation by scavenger reactive oxygen species **(Amany 1994, Dosumu, Nwosu *et al.*, 2006, Aboshora, Lianfu *et al*,. 2014 and Zhang, Li *et al.*, 2019).**

Cardiovascular disease (CVDs) the leading cause of death worldwide, kills about 17 million people each year which represents 30% of all global deaths **(Alwan 2011).**

Hyperlipidemia one of major factors that increase the risk of (CVDs), which is a health disorder occurred when one or more of biochemical tests such as triglycerides, cholesterol, plasma lipoproteins increased at the same time high-density lipoprotein decreased. Any elevation in plasma lipids increased the chances of CVD considerably **(Shattat 2015).**

**El Bcheraoui *et al.* (2014)** reported that majority of population had hypercholesterolemia in age 65 and older. The prevalence of hypercholesterolemia in Saudi Arabia was around (0.7) million males and (0.5) million females (700,000) of the individual were unfamiliar of their illness which could be managed earlier by examination and education promotions in order to modify lifestyle.

The primary treatment for hyperlipidemia is improving lifestyles (diet changes, exercise) and followed by drug therapy all can lower cholesterol levels for those with the form of this disorder **(Nirosha, 2014).** The major medications used to treat hypercholesterolemia such as Statins (Atorvastatine) which works as anti- hypercholesterolemia agents had severe side effects such as deterioration in skeletal muscle tissue, muscle or joint ache, soreness, weakness or liver and kidney problems **(Ramkumar, 2016),** also rash, difficulty breathing; swelling, increase in body temperature, unusual tiredness, and loss of appetite, changes in urine color and amount, jaundice, sore throat and diarrhea **(Woolston, 2019).**

**Habib *et al*., (2014)** determine the influence of oral administration DWE to male rats for one month on hyperlipidemia in nephrotic rats. The study revealed that DWE decreased cholesterol, triglycerides lipoproteins "LDL, VLDL" and increased HDL. The effect of adding 3% of doum to rat's diet to reduce plasma lipid and cholesterol was examined. The study reported that *H. thebaica* has bioactive components which may control lipids profile in rats from elevation, even if they fed high fat diet **(Elhaj and ElBagir, 2016)**

Therefore, the aim of this work is to compare between the effect of DWE and (Statins) hypercholesterolemia medication on hypercholesterolemia rats after 4 weeks of treatment.

## 2. Materials and Methods

### Materials:

### Plant material

Doum (*H. thebaica*) fruit was obtained from local market (Jeddah, Saudi Arabia).

### Kits and chemicals

Enzymatic colorimetric kits for serum total Cholesterol, serum Triglycerides (TG) and High-Density Lipoprotein Cholesterol (HDL-c) were obtained from (Salucea Haansberg, Netherlands). All solvents with high analytical grade were obtained from (Scientific Fisher, Germany). Cholesterol powder and bile acid were purchased from Sigma Chemical Company, USA. Statins (Atorvastatine) were purchased from local pharmacy (Jeddah, Saudi Arabia).

### Rats and diet

Fifty-six male albino rats (160 – 180 g) were obtained from the experimental Animal Unit of King Fahd Medical Research Center, KAU, Jeddah, Saudi Arabia. Basal diet constituents were purchased from (Baghafar Company for Pharmaceutical and Chemical, Jeddah, KSA).

### Methods:

### Preparation of aqueous extract of Doum

Doum fruit powder (10g) was dissolved with (100 ml) of boiling water and vortexed for 30 min. Extract was clarified using filter paper (Whattman No.42) then the extract was concentrated using the rotary evaporator Hahnvapor (HAHNSHIN S & T CO., LTD, South Korea) at 40 °C. The residue was freeze dried by using (Lyophilizer Millorock Bench-Top Freeze Dryer, New York) for 40 hrs and stored in -20°C**(El-Said *et al.*, 2018).**

### Basal diet and cholesterol induction

Basil diet was prepared using Purified Diets for Laboratory Rodents: American Institute of Nutrition (AIN-93G) according to **(Reeves *et al.*, 1993)**. The basal diet consists of the following: Protein (casein) 20%, Fibers (Cellulose) 5%, Sucrose 10%, Corn Oil 4%, Vitamin mixture 1%, Choline Chloride 0.2%, salt mixture 3.5% and the remainder is Corn Starch up to 100%.

### Induction of hypercholesterolemia

Hypercholesterolemia was induced by nourishing rats with diet rich in cholesterol (2%) and bile salt (0.5%) for 4 weeks by using the technique according to **(Pang *et al.*, 2002).**

### Biological Experimental

The experiment was performed on fifty-six male albino rats were divided unsystematically into 7 equal groups, 8 rats/ group. Rats were housed in plastic cages at room temperature maintained at 24±°C, with fixed 12-hour lighting system.

All rats were allowed to free access to basal diet and water for (one week) before starting the experiment for acclimatization. After acclimatization period, the rats were allocated in to following groups.

First group was kept as a control negative group. Groups from (2-7) were fed on hypercholesterolemia diet contain (cholesterol 2% and bile salt 0.5%) for 4 weeks to induce hypercholesterolemia. Groups from (3-7) were given the drug Atorvastatine at a dosage of 40 mg/kg body weight dissolved in distilled water, this dose was calculated from the therapeutic dose (40 mg/day) for human being **(Polska, 2013 and**

**Musorowegomo, 2014)**. Then blood samples were collected to ensure that rats have hypercholesterolemia.

**Table 1: Groups and types of treatment**

| Groups | Type of treatment |
|---|---|
| (1) | Control negative orally given distilled water+ Basal diet only. |
| (2) | Control positive orally given distilled water by gavage + HCD. |
| (3) | Given orally Statins (Atorvastatine) at (40 mg/ kg) + HCD. |
| (4) | Given Doum aqueous extract by gavage at doses of (20 mg/kg) + HCD |
| (5) | Given Doum aqueous extract by gavage at doses of (40 mg/kg) + HCD |
| (6) | Given orally Doum aqueous extract (20 mg/kg) + Statins (Atorvastatine) HCD. |
| (7) | Given orally Doum aqueous extract (40 mg/kg) + Statins (Atorvastatine) HCD. |

In last day of experimental period (4 weeks), all rats were fasted for 12 hours before scarification. Blood samples collected and the serum was separated by centrifugation at 4000 r.p.m for 15 min, clear serum samples were carefully separated using Pasteur pipettes and saved frozen at – 20℃ until biochemical analysis **(Margoni *et al.*, 2011)**. The organs were washed with cold saline solution and dried between two filter papers then weighed and saved for histopathological examination.

**Biological evaluation**

During the experimental period the animals were weighted twice weekly in all groups. The body weight gain (BWG %) was calculation at the end of the experimental period, using the following equation:

**Body weight gain % (BWG %) =** Final b. wt – Initial b. wt / Initial b. wt x 100. Calculation of the relative organs weight was done according to the following equation**: Organ Relative Weight** = Organ weight / Final b. wt x 100.

**Serum biochemical analysis**

Biochemical analyses were measured using different methods as following:

Total cholesterol (TC) estimated according to **(Flegg 1973).** Enzymatic colorimetric GPO-PAP kit was used for measured (TG) as described by **(Fossati and Prencipe, 1982)**. An enzymatic colorimetric kit was used for the determination of HDL-c as described by **(Lopes-Virella et al., 1977).** Low- density lipoprotein -cholesterol (LDL-c) and very low-density lipoprotein-cholesterol (VLDL-c) were calculated according to the equation of **(Friedewald *et al.*, 1972, McNamara *et al.*, 1990)** as follow:

**VLDL-c concentration (mg/dl)**=Triglycerides/5

**LDL-c concentration (mg/dl)** = TC- (HDL-c +VLDL-c)

**Histopathological examination**

Specimens from the halves of liver and heart were taken immediately after weighed the organs of the rats and placed in 10% neutral buffered formalin. The fixed specimens were then trimmed, washed and dehydrated in ascending concentration of ethanol (70%, 80% and 90%) then cleared in xylene and stained with Hematoxylin and Eosin (H E) according to **(Bancroft and Gamble 2008).**

**Statistical analysis**

All the obtained results were analyzed using SPSS for Windows, version 20 (SPSS Inc., Chicago, IL, USA) and Minitab V.16.2.1 (MINITAB Inc., 2010). Collected data was presented as mean ± standard error of mean (SE). Statistical analyses were performed using one-way analysis of variance (ANOVA) according to **(Snedecor and Cochran 1967).** Mean comparison was run using least significant difference (LSD) and Duncan multiple rang test. A P-value less than 0.05 and 0.01 were statistically considered significant and highly significant, respectively.

**Results**

**Effect of DWE on body weight in hypercholesterolemia male rats**:

Table 2 showed that induction of hypercholesterolemia using HCD in a sufficiently great elevated BWG% of rats, and made them hypercholesterolemia. Moreover, therapy with DWE Increased BWG%, on the other hand treatment with statin + DWE reduced BMG% compared to control positive group.

**Effect of DWE on the absolute and relative liver weight in hypercholesterolemia male rats**

Results presented in Table3, showed that treatment DWE w/wo the statin drug significantly reduced the relative liver weight of rats compared to the control (positive) group.

**Table 2: initial body weight, final body weight and (BWG%) of rats' controls compared with groups taken on different dose of DWE with or without Statin drug:**

| Parameters / Groups | Mean ± SE | | |
|---|---|---|---|
| | IBW (g) | FBW (g) | BWG% |
| Group (1) Control (negative) | 171.38 ± 2.1 a | 253.88 ± 3.2 c | 41.1±3.09 a |
| Group (2) Control (positive) | 171.25 ± 4.9 a | 296.75 ± 9.5 ab | 45.53±5.6 a |
| Group (3) Statin (40) + HCD | 169.38 ± 4.5 a | 275.38 ± 9.3 bc | 40.49±5.38 a |
| Group (4) DWE (20 mg/1 kg bw) + HCD | 169.25 ± 4.3 a | 305.88 ± 7.9 a | 47.4±5.35 a |
| Group (5) DWE (40 mg/1 kg bw) + HCD | 168.50 ± 1.4 a | 288.75 ± 8.1 ab | 45.76±4.08 a |
| Group (6) Statin (40) + DWE (20 mg/1 kg bw) + HCD | 171.63 ± 5.8 a | 287.63 ± 5.0 ab | 43±8.17 a |
| Group (7) Statin (40) + DWE (40 mg/1 kg bw) + HCD | 173.50 ± 4.5 a | 295.75 ± 6.4 ab | 42.35±4.89 a |

- Data are presented as Mean ± stander error, (n=8 for each group).
- values with different superscript alphabets indicate significant differences at P< 0,05.
- values with similar or partially similar superscript are non- significant.
- Hypercholesterolemia Diet (HCD) - Doum water Extract (DWE

**Table 3: Effect of oral intake of different dose from DWE with or without statin drug on the absolute and relative liver weight in hypercholesterolemia male rats:**

| Parameters Groups | Absolute Liver Weight (g) | Relative Liver weight (g/100g bw) |
|---|---|---|
| Group (1) Control (negative) | 6.76 ± 0.27 d | 2.66 ± 0.08 c |
| Group (2) Control (positive) | 10.23 ± 0.25 a | 3.47 ± 0.13 a |
| Group (3) Statin (40) + HCD | 8.32 ± 0.38 c | 3.07 ± 0.24 abc |
| Group (4) DWE (20 mg/1 kg bw) + HCD | 8.71 ± 0.29 bc | 2.85 ± 0.07 c |
| Group (5) DWE (40 mg/1 kg bw) + HCD | 9.48 ± 0.45 ab | 3.29 ± 0.17 ab |
| Group (6) Statin (40) + DWE (20 mg/1 kg bw) + HCD | 8.34 ± 0.29 bc | 2.99 ± 0.12 bc |
| Group (7) Statin (40) + DWE (40 mg/1 kg bw) + HCD | 8.84 ± 0.22 bc | 2.99 ± 0.06 bc |

- Data are presented as Mean ± stander error, (n=8 for each group).
- values with different superscript alphabets indicate significant differences at P< 0,05.
- values with similar or partially similar superscript are non- significant.
- Hypercholesterolemia Diet (HCD) - Doum water Extract (DWE)

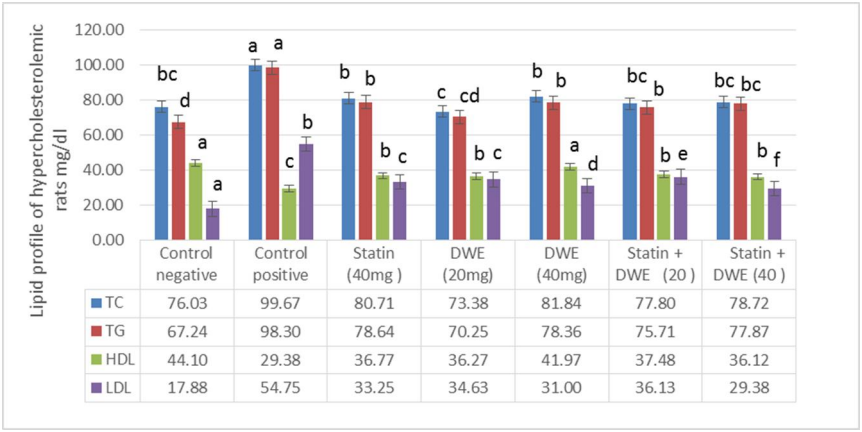


**Figure 1. Effect of DWE on lipid Profile in hypercholesterolemia male rats**

**Effect of DWE on lipid profile in hypercholesterolemia male rats**

Figure1 presents that the highest levels of the total cholesterol (TC), Triglycerides (TG) and LDL-C were clearly seen in group 2 which was fed the HCD, while HDL cholesterol decreased significantly (P<0.05). Therapy of hypercholesterolemia male rats w/wo (Atorvastatin) at (40 mg / kg of body weight) and DWE at doses of (20, 40 mg/kg b. wt) decreased serum levels of total cholesterol, triglyceride and LDL

cholesterol compeer with control positive group. A significant (P<0.05) decrease of TC and TG were observed in group that treat with DWE at dose (20). The level of HDL-C was significant (P<0.05) increase in group 5 which was treat with DWE at dose (40).

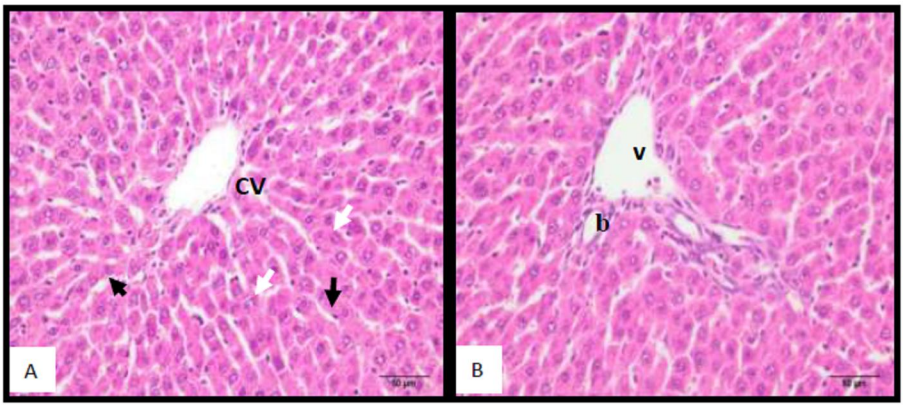


**Figure 2 (A-B):** Photomicrographs of the rat liver-Group I control negative group showing. Hx & E stain -Scale bar 50 µ. A) the polyhedral hepatocytes arranged radially in cords around the central vein (CV) with normal vesicular nuclei (white arrow). B) The portal area shows the normal hepatocytes with their normal vesicular nuclei around the portal vein (V), Bile ducts (b).

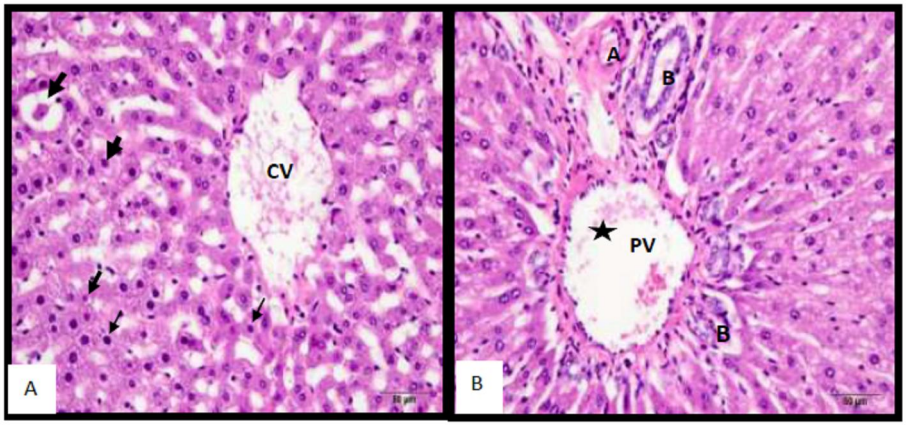


**Figure 3 (A-B):** Photomicrographs of the sections from the rat liver-Group II control positive group. Hx & E - Scale bar 50 µ., A) the hepatocytes around the central vein (CV) have the highly vacuolated cytoplasm with pyknotic nuclei (thin arrows). Notice the necrosed hepatocytes with surrounded by pale area (Thick arrow). B) The cytoplasm of the hepatocyte around the portal area displays the microvascular appearance suggesting the presence of fat droplet accumulation. Notice the focal pale areas around accumulation inflammatory mononuclear cells (*). Notice the multiple bile ducts (B) around a congested portal vein (PV) and the hepatic artery.

**Histopathological investigation:**

**Liver:**

The microscopic examination of the sections from the rat liver in control negative group showed the radially arranged polyhedral hepatocytes around the central vein (CV). The hepatocytes displayed the normal vesicular nuclei with basophilic granules as an indicator for the presence of the rough endoplasmic reticulum. The blood sinusoids had the thin endothelial lining (Fig.2 -A). The portal area had enclosed the portal vein, bile ducts and the hepatic artery. The hepatocytes around the portal areas displayed the normal vesicular nuclei (Fig2 -B).

The histopathological examination of the sections from the rat liver from control positive group revealed the hepatocytes with the highly vacuolated cytoplasm around the central vein. The vacuolation had a well circumscribed appearance suggesting the presence of fat droplets. The nuclei of the hepatocytes appeared pyknotic. Focal hepatocytes were necrosed and surrounded by pale area (Fig.3- A). The cytoplasm of the hepatocyte around the portal area displays the microvascular appearance suggesting the presence of fat droplet accumulation. The focal pale areas around inflammatory mononuclear cells aggregation were noticed. The presence of multiple bile ducts around the congested portal vein and the hepatic artery were frequently noticed (Fig.3- B).

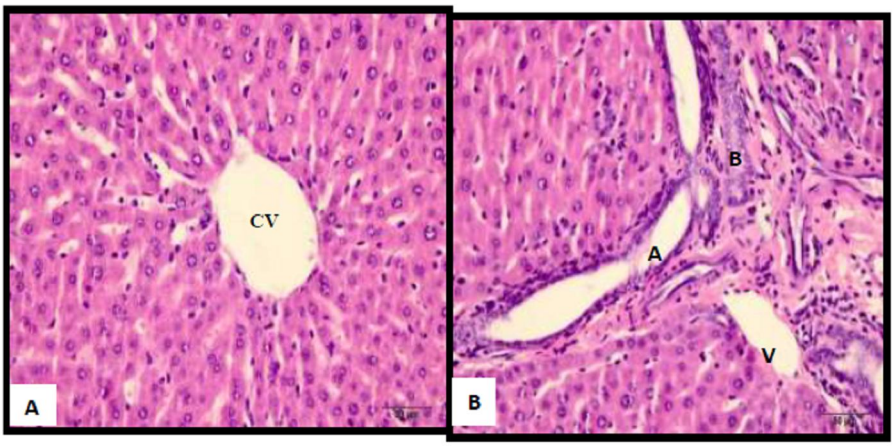


**Figure 4 (A-B):** Photomicrographs of the sections from the rat liver - Group III Statin (40) +HCD. Hx & E stain Scale bar 50 µ. A) the hepatocytes around the central vein (CV) with a similar structure to control. Normal vesicular nuclei of most of the nuclei (→) was noticed. B) The hepatocytes around the portal area are mostly normal hepatocytes with normal vesicular nuclei and a basophilic cytoplasm. Portal vein (PV), Bile ducts (B) and (hepatic artery).

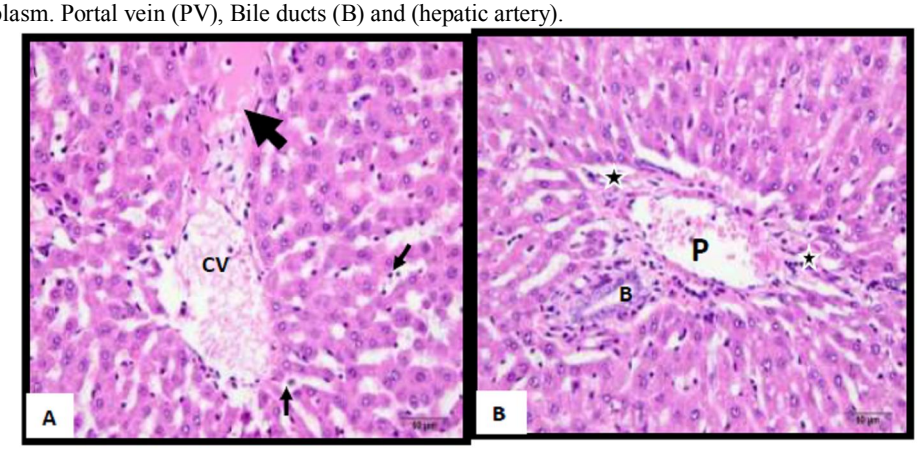


**Figure 5 (A-B):** Photomicrographs of sections from the rat liver-Group IV DWE (20 mg/1 kg bw) + HCD. Hx & E stain Scale bar 50 µ. A mild decreased in the vacuolated cytoplasm of the hepatocytes around a congested central vein (CV). There are sparse focal areas of hyaline degeneration intervene between the hepatic plates. Notice the widespread of the enlarged intrasinusoidal cells (Von Kuepfer cells) (→). B) Many portal areas have a mild congested portal vein (PV) (→). Notice the accumulation of mononuclear inflammatory cells (*) between the liver cell plates and areas of edema (Black star).

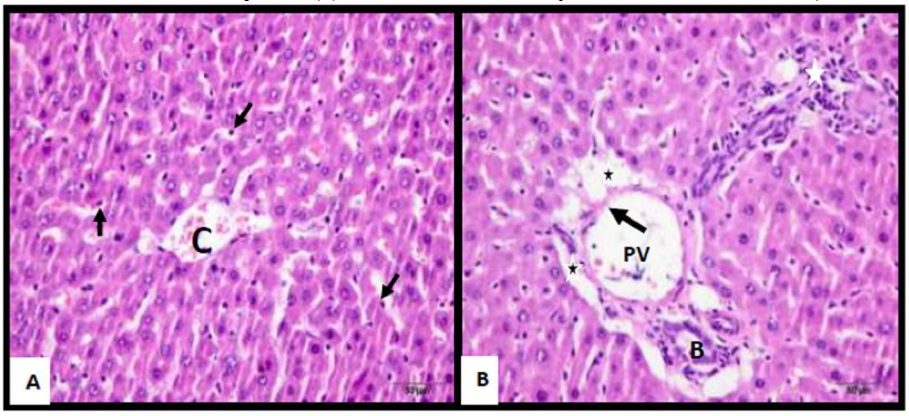


**Figure 6 (A-B):** Photomicrographs of sections from rat liver-Group V DWE (40 mg/1 kg bw) + HCD. Hx & E stain Scale bar 50 µ. A) a moderate decrease in the cytoplasmic vacuolation of the hepatocytes around the central vein (CV) and the surrounding blood sinusoids. Most of the intrasinusoidal cells (Von Kuepfer cells) (→) are prominent. B) Few portal areas have a markedly congested portal vein (PV) with thick wall (→). The apparent marked was decreased in the focal accumulation of mononuclear inflammatory cells between the liver cell plates and areas of edema (Black star).

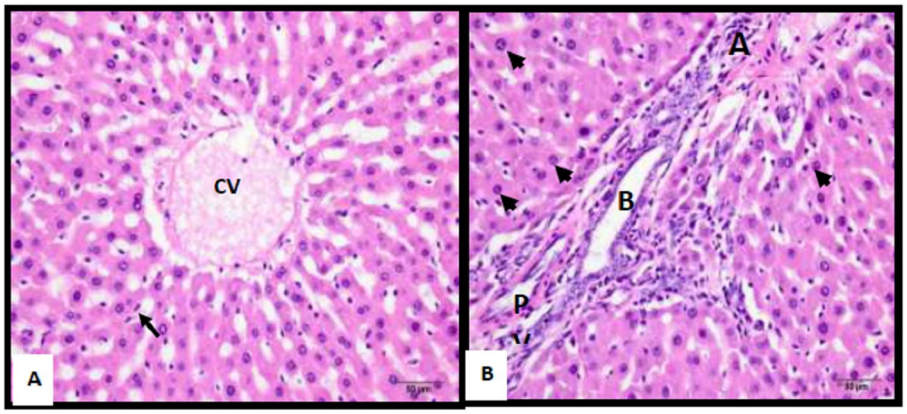


**Figure 7 (A-B):** Photomicrographs of sections from the rat liver -Group VI Statin (40) + DWE (20 mg/1 kg bw) + HCD. Hx & E stain Scale bar 50 µ. A) An apparent marked decrease in the fat deposition in the hepatocytes around the central vein (CV). The hepatocytes have a basophilic cytoplasm with normal vesicular nuclei with prominent nucleoli. Notice the few prominent intrasinusoidal cells (Von Kuepfer cells) (→). B) the hepatocytes around the portal tract has a similar appearance to the treated group III. Notice the normal vesicular basophilic nuclei (→). The Portal vein (PV), Bile duct (B) and Hepatic artery (A).

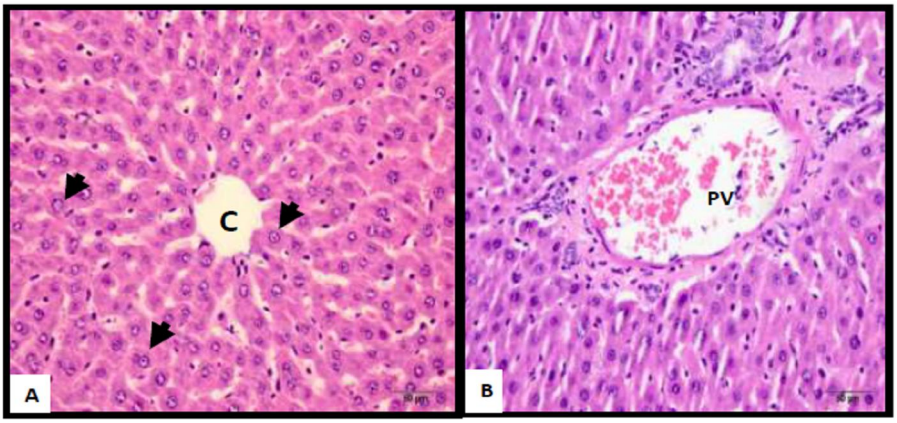


**Figure 8 (A-B):** Photomicrographs of sections from rat liver-Group VII Statin (40) + DWE (40 mg/1 kg bw) + HCD. Hx & E stain Scale bar 50 µ. A) a similar appearance to hepatocytes of the control group around the central vein (CV). B) The hepatocytes around portal area have a similar appearance to the control group.

The microscopic examination of the Group received Statin (40) + HCD) of the sections from the rat liver displayed a similar structure to the control sections. The hepatocytes around the central vein (CV) had normal vesicular nuclei (Fig.4-A). The hepatocytes around the portal area are mostly normal hepatocytes with normal vesicular nuclei and a basophilic cytoplasm (Fig.4- B).

The sections from the rat liver of the Group IV (DWE (20) + HCD) demonstrated a mild decrease in the vacuolated cytoplasm of the hepatocytes around a congested central vein. There are sparse focal areas of hyaline degeneration that intervene between the hepatic plates. There was a widespread of the enlarged intrasinusoidal cells (Von Kuepfer cells) (Fig.5- A). Many portal areas have a mild congested portal veins. The accumulation of mononuclear inflammatory cells was observed between the liver cell plates in a focal manner together with adjacent areas of edema (Fig. 5-B).

The histopathological examination of the rat liver sections from group V (DWE (40) + HCD) had a moderate decrease in the cytoplasmic vacuolation of the hepatocytes around the central vein (CV) and the surrounding blood sinusoids. Most of the intra-sinusoidal cells (Von Kuepfer cells) were prominent. (Fig.6-A). Few portal areas have a markedly congested portal vein (PV) with a thick wall. There was a marked decrease of the focal accumulation of mononuclear inflammatory cells between the liver cell plates and areas of edema (Fig.6 B).

The snapshot in the Figure (7-A) was taken from the sections of the rat liver from Group VI [Statin (40) + DWE (20) + HCD] showed an apparent marked decrease in the fat deposition in the hepatocytes around the central vein (CV). The hepatocytes had a

nearly control appearance with their basophilic cytoplasm and normal vesicular nuclei with prominent nucleoli. Also, the prominent intra-sinusoidal cells (Von Kuepfer cells) were few compared to the hypercholesterolmic group. In the Figure (7- B), the sections showed the hepatocytes around the portal tract with a similar appearance to the treated group III Statin (40) + HCD).

Examinations of the sections from rat liver treated with Statin (40) + DWE (40) + HCD (Group VII), revealed a similar appearance to hepatocytes of the control group around the central vein (CV) (Fig.8-A) and (Fig.8-B).

## 4. Discussion

Hypercholesterolemia, a frequent form of hyperlipidemia, is a metabolic disorder characterized by elevated levels of total cholesterol in the blood. Hypercholesterolemia may develop as a consequence of unbalanced diet, obesity, inherited (genetic) diseases (familial hypercholesterolemia), or other diseases.

Individuals with hypercholesterolemia are at an increased risk for developing cardiovascular disease and doctors usually prescribed statin medications, the most effective cholesterol-lowering drugs. Statin has some side effects that include muscle pain and dysfunction **(Temperly *et al.*, 2019).**

The current study examined the effect of oral intake of DWE w/wo addition of Statin drug, in hypercholesterolemia male rats during (8weeks).

Final body weight (FBW) and body weight gain percent (BWG%) results indicated a significant (P>0.05) increase in all experimental groups compared to initial body weight. Moreover, the final body weight of hypercholesterolemia rats group was significantly (P>0.05) higher compare to control negative group. **El-Gendy *et al.* (2008)** showed that the intake of HFD for 28 days considerably elevated the body weight and produced hyperlipidemia in rats. The elevated (BWG%) could be caused to the elevated level of leptin or the stimulation of ghrelin and peptide YY (PYY) by the HFD **(De Lartigue *et al*,. 2012).**

. The present study shows significant differences between, the administration of DWE at high dose (40 mg) and low doses) 20 mg) in (BWG%) (45,76±4.08, 47.40±5.35) respectively (p= 0.034, p<0.05) when compare to control negative group which has (41.10 ±3.09) and control positive group (45.53±5.60).

This finding was in agreement with those obtained by **(A-Lamer 2012)** the study shows that FBW and BWG% were significantly increased in the rats group that treat with doum extract at a dose 20 mg/kg b.wt.

The increase in body weight could be explained due to the high level of nutrients (carbohydrates, sugar, amino acids, and fatty acids) in doum fruits which has effect on body weight gain in mice **(Aboshora *et al.*, 2017, Mohammed and Zidan, 2018 and El-Ghany *et al.*, 2014)**.

Moreover, management of 200, 400 and 800 mg/kg body weight of aqueous extracts of both stem and bark of *H. thebaica* (L) Mart observed no significant (p > 0.05) variation in feed intake, this could be caused to the absence of tannin in both the stem and bark extracts. The decrease in feed intake and BWG% was showed at the greatest dose of 800 mg/kg of the methanolic fruit pulp extract of the same plant, this could be caused to the tannin content of the methanolic fruit pulp extract of the plant **(Shehu *et al.*, 2015)**. The group that treatment with a statin was significantly (P>0.05) decreased in BWG % compared to the positive control group. statin inhibits Hydroxymethyl glutaryl coenzyme (HMG-COA) reductase, causing a decrease in cholesterol synthesis as well as lowering triglyceride levels and Increasing expression of LDL receptors on hepatocytes **(Csonka *et al.*, 2016 and Ramkumar *et al.*, 2016).**

Results obtained in present study showed that there was a significant (p> 0.05) increased in the relative liver weight on hypercholesterolemia male rats that used different doses from DWE with or without Statin drug when compared to the control negative group. These results were confirmed by histopathological examination of liver which showed the presence of fatty changes of hepatocytes. Our finding are agreement with those results obtained by **(Matos *et al.*, 2005)** who reported that increasing relative liver weight of hypercholesterolemia male rats could be a consequence of the higher fat content on liver.

Feeding hypercholesterolemia rats DWE w/ wo statin significantly (p> 0.05) reduced liver weight compared to control positive group. This result could be explained as follows, the possible mechanism underlying the hepatoprotective properties of the doum fruit is having five flavone glycosides were isolated and identified namely, luteolin 7-O-ßglucuronoide, apigenin 7-O-ß-glucuronoide, luteolin O-ß-glycoside, luteolin 7-O-rutinoside and chrysoeriol 7-O-rutinoside. Antioxidant property is claimed to be one of the mechanisms of hepatoprotective **(Hashim, 1994, Cook, 1998 and El-Ghany and Nanees, 2010).**

In the present study, HCD (positive control group) significantly (p> 0.05) increased TC, TG, LDL-c and a significantly (p> 0.05) decreased HDL-c level compare with control negative group. These results were consistent with the studies of **(Mariee *et al.*, 2012, Adekiya *et al.*, 2018 and Harb *et al.*,2018).**

The results showed significant (p> 0.05) decrease in TC, TG, LDL-C levels accompanied with significant (p> 0.05) increased in HDL-c level in all DWE treatment groups compared with control positive group. These results were consisting with **(El-Gendy *et al.*, 2008 and Bayad, 2016)** studies which report that the administration of DWE were significantly (p<0.05) reduced total cholesterol, triglycerides and LDL-C levels while significantly increasing the concentrations of HDL.

Doum, may protect against increasing the LDL levels even if a HCD is consumed similar finding was reported by **(Elhaj and ElBagir, 2016).** Moreover, lowering triglycerides concentration helps to lower the amount of LDL.

DWE decreased the triglycerides level by reducing lipogenesis or elevating lipolysis and subsequent oxidation of fatty acids into acetyl Co.A which could lessen request for the synthesis of cholesterol and bile acid **(Modu *et al.*, 2000).** Most of the anti-hypercholesterolemia drugs did not decrease triglycerides levels, but the aqueous extracts of doum fruits lower it significantly **(El-Hazmi and Warsy, 2001).** In addition, DWE has hypolipidemic which could be due to the presence of glycosides **(Modu *et al.* 2000)**.

DWE has effect on lowering lipid levels due to the presence of phytochemical components such as phenols, flavonoids, saponins, and tannins that possess significant antioxidant activities **(Shehu, *et al.*, 2015).** It is evident from these findings that doum can serve as a potential source of natural antioxidants, which can help to prevent diseases related to oxidative stress **(Aboshora *et al.*, 2014).** Flavonoids are reported to lower LDL-cholesterol concentrations in hypercholestrolemic animals **(Minato *et al.*, 2003).** The action of flavonoid compounds in preventing the lipase activity has been found, like (Yerba mate) plant from North America had contained flavonoid and phenolic acids which have the ability to prevent the lipase at a concentration of 1.5 mg/mL **(Martins *et al.*, 2010).**

Saponins have been found to form complexes with cholesterol and bile in the intestine treatment indirectly decreasing the cholesterol level in the blood **(Milgate and Roberts, 1995).** They are also, found to prevent pancreatic lipase activity in high-fat diet-fed mice most important to higher fat secretion may because of decreased intestinal absorption of dietary fats **(Daniel *et al.* 2003).** Tannins normalized, TC and LDL level in plasma, They are also, found to inhibition pancreatic lipase activity in high-fat diet-fed mice great significant to higher fat secretion may be due to of reduced intestinal absorption of dietary fats that tannins influence fatty acid catabolism in the liver probably by controlling the hydrolysis of lipoproteins and their selective uptake and metabolism by various tissues **(Velayutham *et al.*,2012).**

In the present work, the Histopathological examination of the sections from liver found that the daily administration of DWE ameliorate reverse the changes occurred by HCD. **Shehata and El-Ghffar (2017)** reported that *H. thebaica* extract has a hepatoprotective activity against mercuric chloride (HgCl2) induced hepatotoxicity in adult male albino rats. Another study conducted by **(Al-Masri and Riyadh 2012)** consumption of doum and methionine has a best significant treatment effect against hepatotoxicity induced by carbon tetrachloride (CCl4) in rats. These results were attributed to the amount of flavonoids such as luteolin, which inhibits lipid oxidation by scavenging free radicals or by other mechanisms, such as singlet oxygen quenching, metal chelation, and lipoxygenase **(Procházková *et al.* 2011).** Total Flavonoids (TFs) from (*Rosa laevigata Michx*) had appropriate potency to develop a hypolipidemic and hepatoprotective activities, of which the levels may be mediated, in part, by enhancing the system of antioxidant defense **(Liu *et al.*, 2010).**

## Conclusion

This study demonstrated that doum water extract possesses a significant reduction in, hypolipidemic and antioxidant effect in hypercholesterolemic rats, as well as overcome most of the histopathology change in liver tissues induced by HCD, Therefore, it recommended that dietary consumption of DWE could be excellent therapy for hyperlipidemia and prevent its complications.

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