Are *Tetraclinis articulata* having a Biological and Histopathological Beneficial Effect on Obese Rats?

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Abstract

Nowadays, the use of herbs or the natural plant for the management of obesity or controlling body weight is interesting. Therefore, the present study was set to investigate the effectiveness of the *Tetraclinis articulata* gum, leaves aqueous extracts, and fruits on obese rats. The experiment was conducted on 28 obese adult male albino rats, randomized into 4 groups (7 rats each). Group one was kept as control obese rats fed high-fat diet (HFD) only, while the other three groups fed accomplished HFD with Arar gum (10% of the diet), orally given of leaves aqueous extract (1ml/100 g b. wt) and fruits (10% of the diet), respectively. The results revealed that control obese rats have a significant ($P<0.05$) increase in body weight gain (BWG), feed intake (FI), feed efficiency ratio (FER), visceral fat weight (VFW) and adiposity index (AI); levels of blood glucose, serum insulin, leptin, TC, TG, TL, LDL-c, VLDL-c, BUN, UA, Cr, MDA, and activity of the liver enzymes, compared to obese rats fed the supplemented HFD with AG, AF or oral administrations of ALE. The significant performance on reducing body weight, VFW and AI; levels of blood glucose, serum insulin, leptin, lipid profile, BUN, UA and Cr was a performance in treated obese rats with the AG, followed by AF and ALE, respectively. While, the superior enhancement result in the serum activity of ALT, AST, ALP, antioxidant enzymes and level of MDA was shown in the treated obese groups by ALE followed by AF and AG, respectively. Microscopic examination of liver sections from control obese rats marked steatosis, portal inflammatory cell infiltration in the hepatic sinusoids and degeneration of the hepatic parenchyma. While, liver sections of treated obese rats with accomplished HFD with AG and AF revealed fewer inflammatory cells infiltration. Oral administration of ALE resulted in fewer random mononuclear inflammatory cells infiltration with slight vacuolar degeneration of the hepatic parenchyma in obese rats. Microscopic examination of kidney sections from control obese rats marked perivascular inflammatory cells infiltration and vacuolar degeneration of renal tubular epithelium in the renal cortex. Meanwhile treated obese rats with AG have apparently normal renal tubules in the renal cortex with mild focal interstitial nephritis. While, kidney sections from treated obese rats with ALE and AF revealed excessive vacuolation of the renal tissue and perivascular edema with fewer inflammatory cells infiltration. Finally, the study concluded that regular intakes of gum, leaves aqueous extract and fruits of Arar, particularly for those who are obese or overweight, in order to reduce the adverse effects of obesity.

Keywords: Obesity; Arar Tree (*Tetraclinis articulate)*; Liver and Kidney Functions; Antioxidant Enzymes.

INTRODUCTION

A body fat abnormal accumulation that has adverse health effects is named obesity. Even though total obesity constitutes a significant risk to a person's health, the dissemination of body fat, especially central and abdominal obesity is more relevant (**Ranasinghe *et al*., 2021**). As well obesity is marred by too much fat depot and a body weight for height is higher than normal. Obesity in the adults at the population level was defined by the WHO as having a body mass index (BMI) of 30 kg/m2 or more (**WHO, 2024**).

Obesity has a long-term health, harmful effects as immediate effects includes insulin resistance, early indicators of cardiovascular disease, hypertension, respiratory problems, an elevated risk of fractures; and psychological effects. Moreover, it is associated with a higher risk of other non-communicable diseases (**WHO, 2004**). The prevalence of obesity is stillness increase at a serious rate, and it has grown into a global epidemic and public health issue. Approximately two billion individuals worldwide are overweight, with over half of them being an obese person **(Powell *et al*., 2021).** According to World Health Organization predicts, this number is increasing, as well as overweight or obese will be caused bad health for nearly 167 million individuals by 2025 (**Hoffman *et al*., 2021**). In line with the data from the 100 Million Health Campaign survey, 39.8% of Egyptian adults aged 30 and older have a body mass index (BMI) of ≥30 kg/m^2. Obesity women (49.5%) was more than men (29.5%). In Egypt, all of the obesity-related disorders put a significant push on the medical and financial systems, which has to pay about 50 billion Egyptian pounds for diseases such as hyperlipidemia, depression, diabetes, high blood pressure, heart diseases, fatty liver and sleep apnea **(Aboulghate *et al*., 2021).**

Medicinal and aromatic herb plants have long been accepted as reliable source of bioactive chemicals that encourage health and as a significant source for novel therapeutic methods. One of this medical plants is *Tetraclinis*, which since the plant's earliest proven use in 1800 B.C., it has been widely utilized for medical uses. *Tetraclinis articulata* is a genus of evergreen coniferous trees in the Cypress family Cupressaceae. It is also known as Arar, Araar, and Sictus tree. In the western Mediterranean region, is referred to as Thuja articulata, Sandarac, Sandarac Tree, or Barbary Thuja (**Annaz *et al*., 2022**).

Tetraclinis is more widespread in North Africa and being used as a source of sandarac resin (**Azémard *et al*., 2017**). The different parts of Sandarac tree (leaves, stems, roots, fruit, and seeds) are used in traditional African medicine to treat a variety of diseases. The various parts of it are prepared as a decoction, infusion, fumigation, and/or paste and administered topically or orally to cure a multiplicity of conditions such as diabetes mellitus, diarrhea, intestinal, respiratory, rheumatism and skin diseases (**Kachmar *et al*., 2021**). As well, in

Eastern Morocco, it is used in conventional medicine to treat allergies, other digestive system illness and dermocosmetics (**Jamila and Mostafa, 2014**); and antibacterial and antioxidant properties (**Jlizi *et al.*, 2018**).The presented study was carried out to investigate the biological and histopathological health benefits of *Tetraclinis articulata* gum, leaves, and fruits on obese rats

MATERIALS AND METHODS

Materials

1- Plant Materials: Dried leaves, fruits and gum of Arar tree were purchased from herbalist shops in Cairo, Egypt and identification by the Herbarium, Botany Department, Faculty of Sciences, Cairo University, Giza, Egypt.

2-Animals: A total number of twenty-eight obese adult male albino rats (Sprague -Dawley strain) weighting (220 ± 10 g) were purchased from the Helwan Colony for Experimental Animals, Ministry of Health and Population, Egypt, after susceptible to diet-induced obesity.

3-Basal Diet Constituents: Casein, cellulose, DL- Methionine, all vitamins and minerals mixtures, L. cystine, and choline bitartrate were obtained from Morgan Company, Cairo, Egypt. However starch, corn oil, and sucrose were obtained from the local market, Egypt.

4- Chemicals and Reagents: All chemicals and reagents for biochemical analysis were purchased from the Gamma Trade Company for Pharmaceutical and Chemical, Dokki, Egypt.

Methods

1- Preparation of High Fat-Diet: All components of the basal diet were mixed together to fulfil the desirable adequate dietary intake for keeping the health state of rats. Concisely, a high-fat diet (HFD) was prepared as described by (**Bhatt *et al.*, 2006**). Briefly, the basal diet was supplied with 59% calories from fat based on sheep and soybean oil, 21% calories from carbohydrate and 20% calories from protein.

2- Preparation of Arar Fruits and Gum: Both Arar fruits and gum were cleaned, sorted, removed all invalid parts, washed from dust, and dried in a hot air oven at 50 ºC for 3 hrs. A grinder mill and sieves were used to obtain a powder particle size of less than 0.4mm. Then, all the milled dried Arar fruits and gum were packaged until further used.

3- Preparation of Arar Leaves Aqueous Extract: According to the methods of **Montassir *et al.*, (2017)**, dried Arar leaves were cleaned from dust and remove all worthless parts. Then, leaves were ground into a grinder and sieves were used to take out a fine powder particle size of less than 0.2mm. One

kilogram of leaves powders was soaked into 10 L of distilled water for 48 hours, and heating at 50º C for 20 minutes. The solution was then filtered using Whatman filter paper no. 4. The filtrate solution was concentrated under vacuum to obtain on concentrated aqueous extracts of Arar leaves and kept in a glass bottle in the refrigerator until used.

4- Experimental Design and Grouping of Rats: All rats were housed in wire cages at the animal house of the Faculty of Home Economics, Helwan University, under controlled environmental conditions of the light/dark cycle (12/12 hr), temperature (22±4°C), and relative humidity (45% to 50%). The supply of food and water was uninterrupted during the experimental period (4 weeks). Rat can be considered the standard for this experiment type since they are susceptible to high fat diet-induced obesity. Prior to the trial study, rats were kept for a week to acclimatize. Subsequently, rats were randomized into four groups, each with seven rats, as follows:

Group (1): Obese rats were kept as a control group and fed on the high fat-diet alone.

Group (2): Obese rats were fed on the supplemented high fat-diet with Arar gum at level of 10% of diet.

Group (3): Obese rats were fed on high fat-diet with given orally aqueous extract from arar leaves (1 ml/100g b.wt.)

Group (4): Obese rats were fed on the supplemented high fat-diet with Arar fruits at level of 10% of diet.

At the end of the experiment period (4 weeks), animals were fasted for 12-hr., except of water and then rats were anaesthetized with diethyl ether and scarified. Blood samples were collected from the posterior vena cava into dry clean centrifuge tubes. Blood samples were left at room temperature to clot, and then centrifuged for 15 minutes at 4000 rpm for serum separation. Serum samples were carefully aspired using a needle and transfers into dry clean test tubes and frozen at -20°C for biochemical analysis. Visceral fat was separated and weighed to estimate the adiposity index.

5- Determination of Feed Intake, Body Weight Gain and Percent Change in Body Weight Gain: Feed intake (FI), feed efficiency ratio (FER), body weight gain and the percent change in body weight gain (BWG %) were determined according to **Bakr and Header. (2014)** using the following equation:

$$\mathbf{BWG\%} = \frac{\text{Final body weight (g)} - \text{Initial body weight (g)}}{\text{Initial body weight (g)}} \times 100$$

FER = Body weight gain (g/day) / Feed intake (g/day).

6- Determination of Visceral Fat Weight and Adiposity Index: Visceral fat weight (g) and adiposity index were determined as described by **Taylor and Phillips, (1996)** using the following formulas:

Visceral Fat Weight (g)= epididymis fat + retroperitoneal fat + abdominal fat

Adiposity index %=total pad fat weights/ Final body weight X 100

7- Biochemical Analysis:

7.1. Determination of Blood Glucose, and Serum Insulin and Leptin Hormone Levels: Blood glucose (BG) levels were determined using a glucose enzymatic kit as described by **Siest *et al.*, (1981).** Serum concentrations of insulin were estimated by using a specific antibody radioimmunoassay (RIA) kits according to the described methods by **Yallow and Bauman, (1983)**. Serum level of leptin hormone was determined using Enzyme-linked immunosorbent assays (ELISA) as described by **Xiong *et al.*, (2005)**.

7.2. Determination of Lipid profile: Serum levels of total lipids (TL), triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c) were determined spectrophotomically according to EnzyChrom ™ Assay Kits instruction manual at 540nm, 570nm, 570nm and at 500 nm individually, as mentioned by **Lutzke and Brauler (1990), and Admundson, Zhou (1999) and Young, (2001),** respectively. While very low density lipoprotein cholesterol (VLDL-C) was calculated using using Friedewald's formula as described by **Friedewald et al., (1972).**

$$\textbf{VLDL-c (mg/ dL) = TG/5}$$

7.3. Determination of Kidney Functions: The Kidney function was inspected through the quantitative determination of serum levels of urea nitrogen (UN), uric acid (UA) and creatinine (Cr) in all rats using colorimetric instructions of QuantiChrom™ Assay Kits as described by **Orsonneau *et al.*, (1992), Walker *et al.*, (1990)** and **Toora and Rajagopal (2002)** respectively. The spectrophotometer was adapted at 520 nm, 590nm and 570nm, respectively.

7.4. Determination of Liver Functions: The serum activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) enzymes were measured calorimetric by utilizing Elabscience® ELISA Kits according to the methods of **Young (2001)** for both ALT and AST and **Roy (1970)** for ALP**.** The spectrophotometer was adapted at 520 nm, 505 nm, 520nm and 620nm, respectively.

7.5. Determination of Serum Oxidative Stress: Malondialdehyde (MDA) was assayed quantitatively in serum using the MDA assay kit by a spectrophotometric method (ABCAM, UK). The MDA in the sample reacts with thiobarbituric acid (TBA) to generate a MDA-TBA adduct. The MDA-TBA adduct is quantified colorimetrically (OD = 534 nm). This assay detects

MDA levels as low as 1 nmol/well colorimetrically **(Draper and Hadley's 1990)**.

7.6. Serum Activity of Antioxidant Enzymes: The serum activity of glutathione peroxidase (GPx), glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD) enzymes were colorimetrically determined using commercial Ela science assay Kits. Optimum wavelengths for determination were 412 nm, 450 nm, 532 nm, 405 nm, respectively, as mentioned by **Hissin and Hilf's (1976**), **Beautler et al. (1963**), **Goth, (1991) and Beauchamp and Fridovich, (1971)**.

8. Histological Examinations: The procedures for the histopathological inspection of the liver and kidney of each rat were performed in line with the referred procedure by **Bancroft and Gamble (2002)**. Concisely, clean liver or kidney samples were dipped separately in buffered formalin (10%) for about one week. Thereafter, the fixed specimens were desiccated in graded ethanolic alcohol from 50 to 100%. Then, specimens were cleared by Xylol, and fixed and deeped in paraffin bulk, then segmented in thickness from 4 to 6 microns and coloured with the Heamtoxylin and Eosin stain for examination.

9. Statistical Analysis: All of the obtained data were analyzed statistically by one-way of variance (ANOVA) using computerized SPSS package program (SPSS 20.00 software for Windows) and expressed as Mean ± Standard Error (SE). Significant differences among means was estimated at $p<0.05$.

RESULTS

1- Effect of Gum, Leaves Extract and Fruits of Arar on BWG, FI and FER in Obese rats: Table 1 illustrate the effect of gum and fruits powder, and leaves extract of Arar on body weight gain (BWG), feed intakes (FI), percent change of body weight gain (BWG%), and FER in obese rats. The results revealed that untreated obese rats (control group) fed on HFD alone have a significant ($P<0.05$) increase in BWG, BWG %, FI and FER, compared to that of obese-rats fed on the supplemented HFD with gum and fruits or that given orally leaves extract of Arar.

Concerning the effect of Arar gum (AG), results approved that the supplemented HFD with it caused a significant decrease ($P>0.05$) in BWG, BWG %, FI and FER, as compared to the obese-groups treated with Arar leaves extract (ALE) or Arar fruits (AF). As well, the supplemented HFD with AF caused a significant decrease ($P>0.05$) in BWG, BWG %, FI and FER, as compared to the obese-groups treated with ALE. Therefore, the current results revealed that the best effect on reducing body weight was shown in treated obese rats with AG, followed by AF and ALE, respectively.

Table (1): The effect of gum, leaves extract *and* fruits of Arar on BWG, BWG %, FI and FER of Obese rats

Groups \ Parameters		IBW (g)	FBW (g)	BWG (g)	BWG %	FI (g/day)	FER (g)
Control obese group		314.00±0.71[a]	390.40±1.52[a]	76.40±1.14[a]	24.33±0.53[a]	13.90±0.42[a]	**0.196±0.04[a]**
Treated obese rats with	**AG (10%)**	314.00±0.71[a]	333.60±1.34[d]	19.60±1.95[d]	6.24±0.91[d]	11.40±0.42[d]	**0.061±0.31[d]**
	ALE (1ml/100gb.wt)	314.20±0.45[a]	350.60±1.34[b]	36.40±1.52[b]	11.58±0.74[b]	12.90±0.42[b]	**0.101±0.01[b]**
	AF (10%)	314.80±0.84[a]	346.60±0.89[c]	31.80±0.84[c]	10.10±0.32[c]	12.00±0.35[c]	**0.094±0.01[c]**

Values are expressed as means ± SD; Values at the same column with different letters are significantly different at P<0.05; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits; **IBW** = Initial Body Weight; **FBW**= Final Body Weight; **BWG%** = Percent Change of Body Weight; **FI**= Feed Intake; **FER=** Feed Efficiency Ratio.

2. Effect of Gum, Leaves Extract and Fruits of Arar on Visceral Fat Weight and Adiposity Index in Obese rats: Table 2 represent the effect of the gum, leaves extract and fruits of Arar on visceral fat weight (VFW) and adiposity index (AI) on obese rats. It was shown that untreated obese rats fed HFD only (control group) have a significant (P<0.05) increase in VFW (g) and AI, compared to obese rats fed on the supplemented-HFD with gum and fruits or that given orally leaves extract of Arar.

The tabulated results also showed that the administration of AG and AF to obese rats caused a significant decrease in the total VFW and AI, compared to treat with that treated with ALE. The rate of improvement in total VFW and AI was more evident in treated obese rats with AG followed by AF and ALE, respectively.

Table (2): The effect of gum, leaves extract *and* fruits of Arar on VFW and AI in obese rats.

Groups \ Parameters		VFW (g)	AI %
Control obese group		12.50±0.82[a]	3.20±0.21[a]
Treated obese rats with	**AG (10%)**	7.97±0.53[c]	2.30±0.16[c]
	ALE (1ml/100gb.wt)	10.00±0.82[b]	2.85±0.18[b]
	AF (10%)	8.00±0.82[c]	2.40±0.22[c]

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits; **VFW=** Visceral fat Weight**; AI=** Adiposity Index.

3. Effect of Gum, Leaves Extract and Fruits of Arar on the Levels of Blood Glucose, and Serum Insulin and Leptin in Obese Rats: The presented data in **Table 3** revealed that the untreated obese rats fed on the HFD alone have a significant (P<0.05) increase in the levels of blood glucose, and serum insulin and leptin hormones, compared to obese rats fed on the supplemented HFD with AG and AF or that orally given ALE. While, feeding obese rats on the supplemented HFD with AG had significant (P<005) decrease in the levels of blood glucose, and serum insulin and leptin hormones, compared to obese rats fed the supplemented HFD with AF or that orally given ALE. On the other hand, the supplemented HFD with AF caused a significant decrease (P> 0.05) in the levels of blood glucose, and serum insulin and leptin hormones in obese rats, compared to orally given of ALE to obese rats.

Consequently, the present outcome demonstrates that AG, followed by AF and then ALE, respectively, resulted in a significant enhancement in the levels of blood glucose, and serum insulin and leptin hormones in obese rats.

Table (3): The effect of gum, leaves extract *and* fruits of Arar on the levels of blood glucose and serum insulin and leptin in obese rats.

Parameters / Groups		Blood Glucose (mg/dl)	Insulin (mg/dl)	Leptin (ng/mg)
Control obese group		218.60±1.14[a]	6.87±0.05[a]	14.10±0.20[a]
Treated obese rats with	**AG (10%)**	108.40±0.89[d]	1.73±0.21[d]	4.86±0.34[d]
	ALE (1ml/100gb.wt)	155.27±0.71[b]	5.06±0.87[b]	9.37±0.49[b]
	AF (10%)	136.85±1.41[c]	4.29±0.27[c]	7.33±0.49[c]

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits.

4. Effect of Gum, Leaves Extract and Fruits of Arar on the Lipids Profile in Obese Rats: To discover the effect of AG, ALE and AF on the lipids profile in obese rats, the parameters of serum TC, TG, TL, HDL-c, LDL-c and VLDL-c levels were used. The results in **Table 4** show that obese rats fed on HFD Onley have a significant (P<0.05) increase in the serum concentrations of TC, TG, TL, LDL-c and VLDL-c levels, and a decrease in HDL-c levels, compared to obese rats fed on the supplemented HFD with AG and AF or that orally given ALE.

With regard to the effect of supplemented HFD with AG, the results showed a significant decrease (P> 0.05) in the mean values of serum TC, TG, TL, LDL-c and VLDL-c levels, and increase in HDL-c levels, compared to obese rats fed on the supplemented HFD with AF or that orally given ALE. However, AF caused a significant decrease in the serum levels of TC, TG, TL, LDL-c and VLDL-c and increase HDL-c level, compared to effect of ALE on obese rats. the rate of improvement in the serum levels of the above tested parameters was more evident with AG followed by AF and ALE, respectively.

Table (4): The effect of gum, leaves extract *and* fruits of Arar on lipid profile in obese rats.

Parameters / Groups		TC (mg/dl)	TG (mg/dl)	TL (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
Control obese group		119.08±0.85[a]	130.60±1.05[a]	543.29±3.62[a]	12.77±0.80[d]	53.59±1.39[a]	**26.08±0.33[a]**
Treated obese rats with	**AG (10%)**	74.86±0.86[d]	92.25±0.75[d]	340.71±3.97[d]	29.88±0.54[a]	23.80±0.84[d]	**18.51±0.45[d]**
	ALE (1ml/100g b.wt)	103.80±0.27[b]	109.94±0.93[b]	408.00±1.8[b]	24.41±0.99[b]	40.16±0.73[b]	**22.05±0.32[b]**
	AF (10%)	90.54±1.28[c]	99.00±0.71[c]	375.00±3.37[c]	18.04±0.99[c]	32.62±0.83[c]	**19.90±0.56[c]**

Values are expressed as means ± SD; Values at the same column with different letters are significantly different at P<0.05; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits; **TC**= Total cholesterol; **TG** =Triglyceride; **TL**= Total Lipid; **HDL-c** = High Density Lipoproteins Cholesterol; **LDL-c=** Low Density Lipoproteins Cholesterol; **VLDL-c=** Very Low Density Lipoproteins Cholesterol.

5- Effect of Gum, Leaves Extract and Fruits of Arar on Kidney Functions in Obese Rats: As shown in **Table (5)**, the serum concentrations of BUN, UA and Cr were reduced significantly (P<0.05) in obese rats fed on the supplemented HFD with AG and AF or that orally given ALE, compared to obese rats fed HFD alone. On the other hand, feeding rats on accomplished HFD with AG caused significant reduction in the serum levels of BUN, UA and Cr, compared with feeding obese rats on the supplemented HFD with AF or oral administrations of ALE. Additionally, the complemented HFD with AF resulted in a significant decrease in serum levels of BUN, UA and Cr, compared with the supplemented HFD with ALE. It was shown that the superior improvement result in the serum concentration of BUN, UA and Cr in obese rats was shown in the treated groups by AG followed with AF and ALE.

Table (5): The effect of gum, leaves extract *and* fruits of Arar on the serum levels of BUN, UA and Cr in obese rats.

Parameters / Groups		BUN (mg/dl)	UA (mg/dl)	Cr (mg/dl)
Control obese group		7.79±0.53[a]	3.22±0.51[a]	9.01±0.40[a]
Treated obese rats with	**AG (10%)**	3.91±0.03[d]	1.01±0.10[d]	4.50±0.47[d]
	ALE (1ml/100gb.wt)	6.30±0.20[b]	2.04±0.03[b]	7.04±0.18[b]
	AF (10%)	5.00±0.47[c]	1.80±0.10[c]	5.46±0.15[c]

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits; **BUN**= Blood Urea Nitrogen; **UA**= Uric Acid; **Cr**= Creatinine.

6- Effect of Gum, Leaves Extract and Fruits of Arar on Liver Functions in Obese Rats: The results in **Tables 6** illustrate the effect of the AG, ALE and AF on the serum activities of ALT, AST and ALP enzymes in obese rats. It revealed that HFD only caused a significant increase in the serum activities of

AST, ALT and ALP enzymes in obese rats, compared to that caused by the supplemented HFD with AG and AF or oral administration of ALE in obese rats. On the other hand, feeding obese rats on HFD with the oral administration of ALE caused a significant reduction in the serum activity of ALT, AST and ALP enzymes, compared with that feeding on the supplemented HFD with AG and AF. Additionally, the complemented HFD with AF resulted in a significant decrease in the serum activity of ALT, AST and ALP enzymes, compared with the supplemented HFD with AG. As shown, the better enhancement in the serum activity of ALT, AST and ALP enzymes was shown in the treated obese groups with ALE followed with AF and AG.

Table (6): The effect of gum, leaves extract *and* fruits of Arar on the serum activities of ALT, AST and ALP enzymes in obese rats.

Parameters / Groups		ALT (µ/L)	AST (µ/L)	ALP (µ/L)
Control obese group		84.27±0.93[a]	97.60±1.14[a]	7.59±0.18[a]
Treated obese rats with	**AG (10%)**	72.42±0.43[b]	82.40±0.55[b]	5.59±0.44[b]
	ALE (1ml/100gb.wt)	50.21±1.07[d]	64.82±1.04[d]	3.36±0.21[d]
	AF (10%)	61.83±0.23[c]	70.26±0.42[c]	4.46±0.50[c]

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits; **ALT**= Alanine Aminotransferase; **AST**= Aspartate Aminotransferase; **ALP**= Alkaline Phosphatase.

7- Effect of Gum, Leaves Extract and Fruits of Arar on the Serum levels of MDA and Activity of GPx, CAT and SOD enzymes in Obese Rats: The results of the effect of supplemented HFD with AG, AF powder and oral administration of ALE (*Tetraclinis articulate*) on the serum level of MDA and the activities of GPx, CAT and SOD enzymes in the experimental obese rats are recorded in **Table 7**

Results showed that non-treated obese rats (control group) fed on HFD alone have a significant increase in $p<0.05$ in the serum level of MDA, compared with those of treated obese rats fed on the supplemented HFD with AG, AF powder and oral administration of ALE as shown in **Table 7**. As well, the obtained results revealed that oral administration of ALE caused significant ($p<0.05$) decrease in the serum MDA level, compared to the supplemented HFD with AG and AF in obese rats.

As shown in **Table 7**activity of the antioxidant enzymes (GPx, CAT and SOD) was significant ($p<0.05$) decrease in obese rats fed on HFCD alone, compared to obese rats fed on the supplemented HFD with AG, AF powder and oral administration of ALE. Nevertheless, results demonstrate that obese rats that treated with oral administration of ALE have a significant ($p<0.05$) increase in the activity of antioxidant enzymes, compared to that fed on the supplemented HFD with AG or AF.

The assessment of amelioration in the serum levels of MDA and activity of antioxidant enzymes was superior with oral administration of ALE followed by AF and AG, respectively, in obese rats.

Table (7): The effect of gum, leaves extract *and* fruits of Arar on the serum levels of MDA and activity of GPx, CAT and SOD enzymes in obese rats.

Parameters / Groups		MDA (ng/ml)	GPx (ng/ml)	CAT (ng/ml)	SOD (ng/ml)
Control obese group		4.39±0.30[a]	2.06±0.08[d]	1.19±0.14[c]	0.93±0.02[d]
Treated obese rats with	**AG (10%)**	3.09±0.04[b]	3.41±0.37[c]	2.00±0.08[b]	1.76±0.11[c]
	ALE (1ml/100gb.wt)	1.53±0.19[d]	5.11±0.16[a]	3.07±0.64[a]	3.10±0.11[a]
	AF (10%)	2.77±0.23[c]	4.26±0.32[b]	3.06±0.24[a]	2.31±0.27[b]

Values expressed as means ± SD; Means with different letters in each column are significantly differs at p< 0.05. Values expressed as means ± SD; **AG**= Arar Gum; **ALE=** Arar Leaves Extract; **AF**= Arar Fruits; **MDA=** Malondialdehyde; **GPx=** Glutathione Peroxidase; **CAT=** Catalase Peroxidase; **SOD**= Superoxide Dismutase

8- Histopathological Examination

8.1- Histopathological Examination of Liver: Microscopic examination of liver sections from untreated obese rats (control rats) marked steatosis, portal and variable inflammatory cell infiltration in the hepatic sinusoids, as well as degeneration of the hepatic parenchyma (**Photo 1**). As shown in **Photo 2**, liver sections of treated obese rats by AG (group 2) showing fewer portal mononuclear inflammatory cells infiltration. Liver sections of treated obese rats by ALE (group 3) showing random mononuclear inflammatory cells infiltration and vacuolar degeneration of the hepatic parenchyma (**Photo 3**). While, liver sections of treated obese rats by AF (group 4) showing numerous multifocal inflammatory cells infiltration (**Photo 4**).

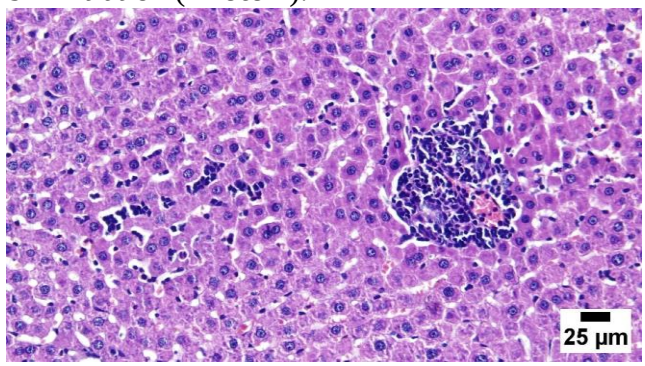

Photo 1: Photomicrograph of liver sections of control obese rats (group 1) showing steatosis in several examined sections portal inflammatory cells infiltration with variable inflammatory cells infiltration in the hepatic sinusoids (H&E).

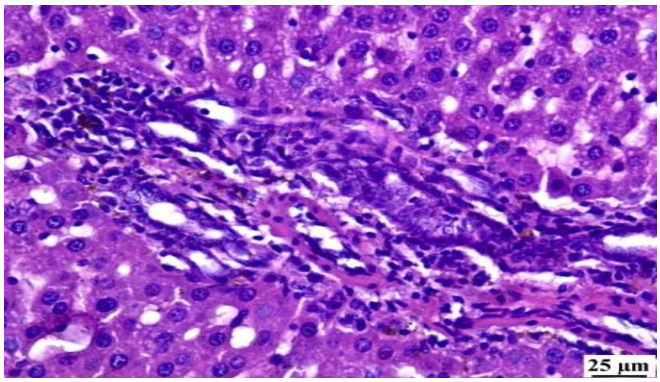

Photo 2: Photomicrograph of liver sections of treated obese rats by AG (group 2) showing fewer portal mononuclear inflammatory cells infiltration (H&E).

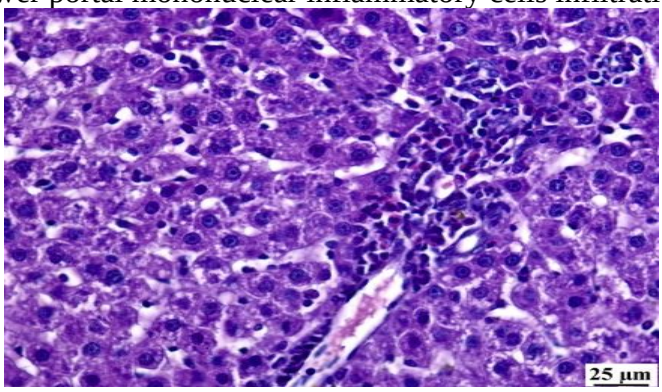

Photo 3: Photomicrograph of liver sections of treated obese rats by ALE (group 3) showing random mononuclear inflammatory cells infiltration and vacuolar degeneration of the hepatic parenchyma (H&E).

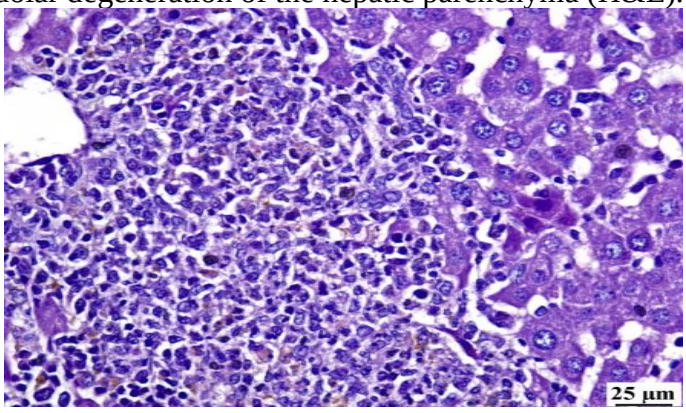

Photo 4: Photomicrograph of liver sections of treated obese rats by AF (group 4) showing numerous multifocal inflammatory cells infiltration (H&E).

8.2. Histopathological Examination of kidney: Microscopic examination of kidney sections from untreated obese rats (control group) marked perivascular inflammatory cells infiltration and vacuolar degeneration of renal tubular epithelium in the renal cortex (**Photo 5**). Meanwhile, examined kidney sections of treated obese rats with AG (group 2) showed apparently normal renal tubules in the renal cortex with mild focal interstitial nephritis (**Photo 6**). While, kidney sections of treated obese rats with ALE (group 3) showing excessive vacuolation and perivascular edema with fewer inflammatory cells infiltration of the renal tissue (**Photo 7**). As shown in **Photo 8**, kidney sections of treated obese rats with AF (group 4) have perivascular edema, inflammatory cells infiltration and vacuolar degeneration of renal tubular epithelium.

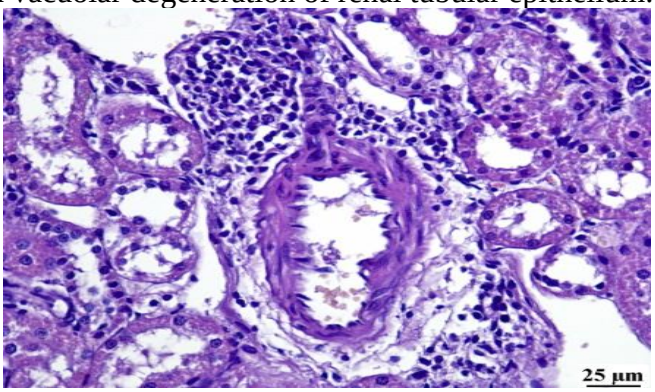

Photo 5: Photomicrograph of kidney sections of control obese rats (group 1) showing perivascular inflammatory cells infiltration and vacuolar degeneration of renal tubular epithelium in the renal cortex (H&E).

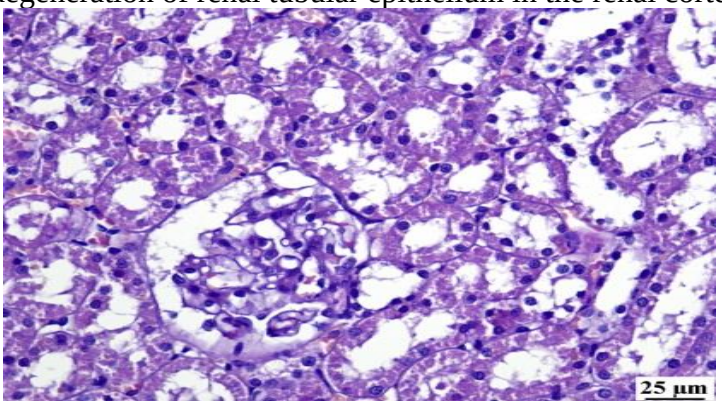

Photo 6: Photomicrograph of kidney sections of treated obese rats with AG (group 2) showing apparently normal renal tubules in the renal cortex with mild focal interstitial nephritis (H&E).

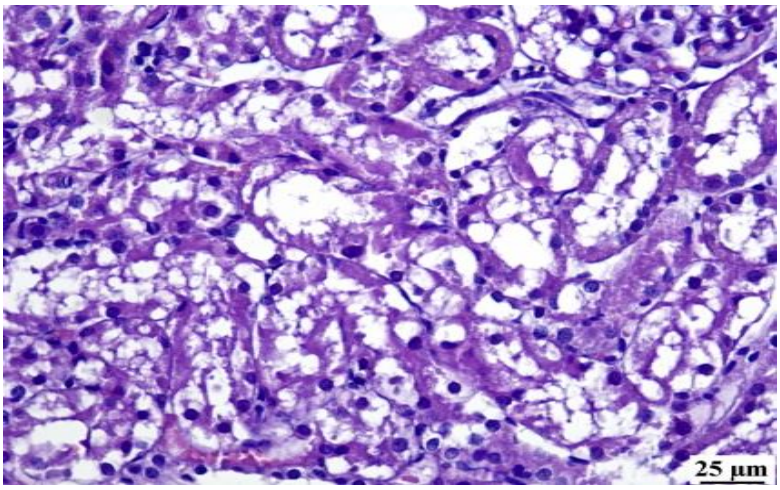

Photo 7: Photomicrograph of kidney sections of treated obese rats with ALE (group 3) showing excessive vacuolation and perivascular edema with fewer inflammatory cells infiltration of the renal tissue (H&E).

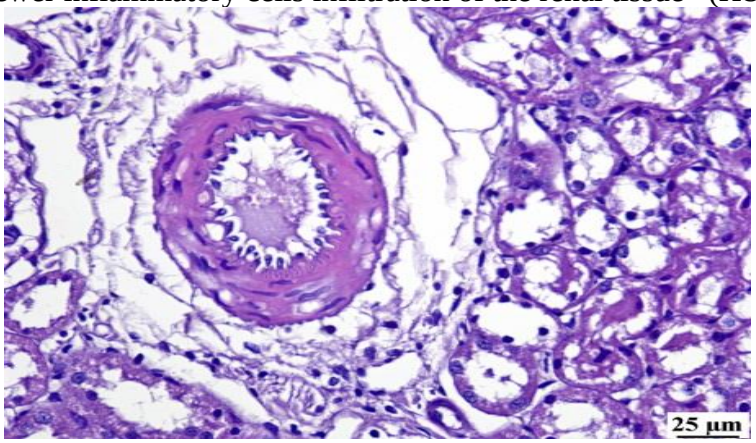

Photo 8: Photomicrograph of kidney sections of treated obese rats with AF (group 4) showing perivascular edema, inflammatory cells infiltration and vacuolar degeneration of renal tubular epithelium (H&E).

Discussion

Obesity is described as an abnormal or excessive buildup of fat that poses a health concern. Nowadays, there are more obese people than underweight ones, making obesity one half of the double burden of malnutrition. Obesity and overweight are significant risk factors for many chronic illnesses, including

cardiovascular illnesses like heart disease and stroke, which are the world's leading causes of death **(WHO, 2021).**

Due in large part to their naturally occurring bioactive chemicals that can aid in weight loss by addressing various elements of metabolism, medicinal plants have demonstrated encouraging results in the treatment of obesity. *Tetraclinis articulata*, often called the Sandarac tree or Mediterranean cypress is used in a variety of herbal and plant extracts and its historical usage in traditional medicine **(Saber *et al*., 2023).** Therefore, we studied the effects of Tetraclinis articulata gum, leaves, and fruits on obese model rats from a biological and histological standpoint.

The obtained data revealed that untreated obese-rats fed on HFD have a significant increases ($P<0.05$) in FI, FBW, BWG, FER, VFW and AI, compared to that of the treated obese- rats fed on the supplemented-HFD with AG or AF or that given orally ALE. These outcomes were in arrangement with **Rezq, (2017)** and **Ogungbemi *et al*., (2017)** who found a significant increment in BW of rats fed on HFD. Further, **Abdulrahman *et al*., (2020)** informed that feeding rats on HFD caused a significant increase in BW, compared to that of feeding rats on the basal diet.

As suggested by the obtained results of increasing in VFW and AI, it confirms that obesity is characterized by augmented adipose tissue weight that consequence from both increasing fat cell number and fat cell size (**Lafontan and Langin, 2009**). It known that abiogenesis is a component of the adipocyte differentiation action from pre-adipocyte precursors into mature fat cell with the development and increase of subcellular lipid bead (**Ali *et al*., 2013**). This process is associated with the development of obesity. As well, excess energy uptake and lower energy expenditure derive in abnormal disproportionate growth of white adipose tissue (WAT), which can lead to the progress of obesity in rats (**Jo *et al*., 2009**). Regarding to effect of AG, AF and ALE on BW, FI and FER the cureent results revealed that the supplemented HFD with AG or AF or oral admenistration of ALE caused a significant decrease ($P>0.05$) in BWG, BWG %, FI and FER, as compared to the control obese-groups fed on HFD only. The obtained results may be attributed to that sandarac tree is rich in bioactive compounds such as flavonoids, terpenoids, phenolic acids, and essential oils, that have effects on obesity and metabolic health (**Khatib *et al*., 2022**) and support the development of fat and insulin resistance **Chouhan and Guleria, (2020)**. These results are agree with **Yang *et al*., (2017)** who found that rats fed a high-fat diet, dietary flavonoids can prevent weight gain, fat deposition, and hypertriglyceridemia. Additionally, **Singh *et al*., (2016)** and **Abd Elmeged and Alzahrani, (2024)** observed that supplemented diet with arar fruits declined BW. As well, **Dinda *et al*., (2020)** shown that flavonoids from herbal and dietary plants have potential advantages for treating and preventing obesity and its link to metabolic diseases. Where, one of the main ways that flavonoids prevent obesity is by reducing the absorption of fat and carbohydrates. Furthermore, blocking the digestive enzymes necessary for the breakdown of lipids and carbohydrates may directly impair their absorption and

digestion (**Pan *et al*., 2018**). This results aligns with **Song *et al*., (2019)** who found that flavonoids, which are abundant in plants and active substances with a range of biological roles have been shown to be effectively in decrease obesity and associated metabolic disorders. Additionally, flavonoids have anti-obesity qualities that may be utilized in functional foods or side-effect-free anti-obesity drugs. Flavonoids may inhibit weight gain in a number of ways, either directly or indirectly through their physiologically active metabolites. In addition to their functional characteristics, which include controlling the expression and activity of several enzymes involved in the metabolism of fats and carbohydrates, flavonoids also have health-promoting properties (antioxidative,anti-inflammatory, and metabolic effects) (**Berger *et al*., 2015**).

One of the risk factors for diabetes linked to insulin resistance is obesity. Adipose tissue in obese people releases more non-esterified fatty acids, glycerol, hormones, and pro-inflammatory cytokines, all of which may contribute to the development of insulin resistance. Insulin resistance is also influenced by endoplasmic reticulum stress, oxidative stress, lipodystrophy, adipose tissue hypoxia, and genetic background **(Wondmkun, 2020).** Insulin resistance in humans can be linked to lifestyle and can be notice more as a cause of lipid deposition in a caloric excess. Insulin resistance is associated with a number of metabolic disorders such as obesity, hyperlipidemia, and hypertension (**Unger and Scherer, 2010**). Numerous evidences indicated that in experimental animals, high-fat diets resulted in disturbance in glucose metabolism and impaired glucose tolerance (**Vessby, 2000**).

The obtained results documented that obese rats fed on the HFD alone have a significant ($P<0.05$) increase in the levels of blood glucose, and serum insulin and leptin hormones, compared to obese rats fed on the supplemented HFD with AG and AF or that orally given ALE. This result was agreed with **Kusunoki *et al*., (2021)** who showed hyperglycaemia, dyslipidaemia and hyperinsulinaemia in rodents fed a high-fat diet. **Srinivasan *et al*., (2004)** revealed that the feeding on high-fat diet for a period of 30 days increased levels of serum insulin and insulin resistance. Some previous studies revealed that hyperinsulinemia and insulin resistance are common features of obesity in experimental animals (**Amin and Nagy, 2009**).

In contrast, the current study approved that the supplemented diet with AG or AF or oral administration of ALE caused a significant decrease ($P<0.05$) in blood glucose, and serum insulin and leptin hormones, compared to control obese group. This result was agreed with **Eksi *et al*., (2020)** who demenstrated that the presence of diterpenes in arar gum and has utilized diterpenes for a number of conditions, including antidiabetes. As well the diterpenoids have antihyperglycemic, anti-inflammatory, and other properties (**Wang *et al*., 2018**). This consistent with **Yassir *et al*., (2022)** who proved that characteristics of sandarac gum's protection Recently, there has been a lot of interest in discovering new plant-based antioxidants to protect the body against diseases including diabetes, inflammation, and other disorders caused by free radicals.

Additionally, the effect of ALE on blood glucose and serum insulin level due to the presence of a compound tannins in it that have been characterized as anti-hyperglycemic. Also, due to the presence of flavonoids, which are useful components. Because they improve oxidative and altered glucose metabolisms, several flavonoids have antidiabetic effects (**Pinent *et al.*, 2004**). As well, through mediators of the insulin-signaling pathways, including GLUT-4 translocation, PI3K (phosphoinositide 3-kinase), and p38 MAPK (mitogen-activated protein kinase) activation, they have been shown to improve glucose uptake. Phenolic substances have been linked to a decrease in glycemia (blood glucose levels) through mechanisms such decreased nutritional absorption As well the direct effect on increases insulin activity (**Anderson and Polansky, 2002**). According to **Jouad *et al.*, (2001)** the Arar leaves are mostly utilized to treat rheumatism, diabetes, hypertension, intestinal, respiratory, and stomach disorders. These results are consistent with **(Bouadid *et al.*, 2022)** who reported that Tetraclinis articulata leaves extract has a strong ability to reduce glucose levels. As well, **Chan ChungHung *et al.*, (2012)** indicated that Arar leaves contain catechin which acts on decreasing the high blood glucose levels. These results could be explained by that the catechin function on stimulating insulin production from the remaining β-cells.
On the other hand **Gray *et al.*, (2000)** demonstrated that by either enhancing glucose absorption metabolism or preventing hepatic gluconeogenesis, catechin may have an insulin-like action on peripheral tissues.

Regarding the effect arar fruits on blood glucose and serum insulin levels, the present study agreed with **Abd Elmeged and Alzahrani, (2024)** who observed a decrease in glucose levels in rodents fed supplemented diet with arar fruits. Additionally, **Raina *et al.*, (2019)** reported that arar fruits have anti-inflammatory, hypoglycemic, and hypolipidemic properties in mice. The antidiabetic effect of arar fruits may be related to its essential oil and antioxidant content which inturn improves insulin action. This consistent with **Chouhan and Guleria, (2020)** who proved that flavonoids have anti-inflammatory and potent antioxidant qualities. It has been demonstrated that flavonoids can reduce inflammation and oxidative stress, both of which are often increased with obesity. Arar fruits flavonoids may enhance metabolic health by reducing pro-inflammatory indicators that fuel insulin resistance and fat storage. As well, **Gentile *et al.*, (2018)** reported that flavonoids have been shown to have a variety of biological properties, including antioxidant activity, and may lower the risk of serious chronic illnesses. The potential benefits of flavonoids in reducing oxidative stress and associated inflammatory conditions, which may help combat obesity and associated co-morbidities such as type 2 diabetes mellitus and cardiovascular disease. In addition, Arar fruits content of vitamin C may had a positive benefits on type 2 diabetic patients' lipid and glucose metabolism (**Paolisso *et al.*, 1995**). Consuming antioxidants, including vitamin C, may assist to repair the antioxidant defense system by lowering the oxidative stress linked to diabetes (**Shamsi *et al.*, 2006**). This aligns with

Abdel-Wahab *et al*., (2002) found that giving mice VC improved their insulin resistance.

The leptin hormone can regulate food intake, body mass, lipolysis, proinflammatory immune responses, and embryonic growth. The obese (ob) gene produces leptin, which binds to and activates its cognate receptor, the leptin receptor (LEP-R), after being synthesized and secreted from fat cells in white adipose tissue. The distribution of LEP-R promotes the pleiotropic effects of leptin and is essential for controlling body mass through a negative feedback loop between the hypothalamus and adipose tissue. Increased total body mass, overnutrition, and decreased satiety are the hallmarks of leptin resistance. This frequently results in obesity, which lessens the therapeutic benefit of exogenous leptin. Combining leptin sensitizers with leptin therapy may therefore aid in overcoming this resistance and, as a result, obesity **(Obradovic *et al*., 2021).**

The current study showed that supplemented diet with arar gum or fruits or oral admenistration of arar leave extrat caused a significant decrease in serum leptin levels ($P<0.05$) compared to control obese-group.

One possibility mechanisms is the positive regulation of insulin signaling. As well **Danielewski *et al*., (2021)** revealed that several flavonoids have been reported to possess anti-adipogenic and lipogenic activities, regulating leptin secretion. Additionally, inhibition of oxidative stress and regulation of gut microbiota by flavonoids might also play a role for its effects on leptin **(Kowalska *et al*., 2021). Liu *et al*., (2022)** reported that flavonoid significantly decreased circulating leptin levels and suggested that flavonoid might be an effective strategy for improving the circulating adiponectin to leptin ratio, and consequently might be beneficial for obesity and related disorders. Another study found that inhibiting glucose uptake reduced the production and secretion of leptin in rat adipocytes **(Mueller *et al*., 1998).** Additionally, vitamin c dramatically reduced leptin release in a concentration-dependent manner, particularly in cells activated by insulin and decreased leptin release, altered the expression of several significant proteins linked to obesity in primary rat adipocytes, and inhibited some markers of glucose and lipid metabolism. Vitamin C–glucose transport competition may be the cause of the decrease in glucose absorption. This might potentially result in the inhibition of leptin secretion, which could then fuel the observed inhibition of lipolysis (**Garcia-Diaz *et al*., 2010**).

Obesity increases fasting plasma triglycerides, total cholesterol and LDL and low HDL cholesterol which are some of the risk factors that obesity raises. The existence of the small dense LDL phenotype are novel lipid-dependent metabolic risk factors linked to obesity. A pro-inflammatory gradient that may have its origins in the adipose tissue itself and directly impact the endothelium may be linked to all of these lipid abnormalities, which are common characteristics of the metabolic syndrome **(Klop *et al*., 2013).** The results revealed that control obese rats fed on HFD only have a significant ($P<0.05$) increase in the serum concentrations of TC, TG, TL, LDL-c and VLDL-c levels, and a decrease in HDL-c levels, compared to obese rats fed on the

supplemented HFD with AG and AF or that orally given ALE. Furthermore, **Rezq and El-Khamisy, (2011)** exhibit that nourishing rats on the HFD results in dyslipidemia characterized by the increasing in serum TL, TG, TC, VLDL, and LDL-c and decreasing HDL-c levels. As well, **Rezq *et al*., (2017)** exhibit that feeding rats on the HFD results in significant increase in serum concentrations of TG, TL, TC and LDL-c and decrease HDL-c levels.

With regard to the effect of supplemented HFD with AG or AF or oral administration of ALE the results showed a significant decrease ($P > 0.05$) in the mean values of serum TC, TG, TL, LDL-c and VLDL-c levels, and increase in HDL-c levels, compared to control obese rats fed on the HFD. This results consistent with **Romero-Noguera *et al*., (2014)** who reported that the Arar gum has anti-lipogenesis effect due to the fact that it include communic acid. Communic acid makes up about 70% of the resin and its biological functions include hypolipidemia. As well, **Nazir *et al*., (2020)** showed that arar leaves raised HDL-c and reduced serum levels of TC, TG, and LDL. The observed decrease in plasma triglyceride levels may be due to catechin's potential to inhibit pancreatic lipase, which would delay the absorption of fat.

In the study of **Ghudhaib, (2014)** serum TG, total cholesterol, and HDL-c levels were measured in treated mice given varying amounts of catechin for one to three weeks. The findings demonstrate that both low and high doses of catechin helped the treated mice achieve normal TG values by the second week of treatment, while both low and high doses of catechin extract helped the mice achieve normal cholesterol values by the third week of treatment. This results agreed with **Afolabi *et al*., (2015)** who showed that catechin dramatically decreased levels of LDL, phospholipids, triglycerides, and cholesterol by promoting the activity of enzymes involved in cholesterol catabolism, catechin may have stopped the lipid from accumulating. Additionally, catechin may be able to inhibit pancreatic lipase, which would delay the absorption of fat and perhaps lower the content of plasma triglycerides (**Afolabi *et al*., 2016).** As well the presence of sterols in the arar leaves extract may be related to lower LDLs or cholesterol levels by preventing the intestines from absorbing cholesterol as indicated by **Alamgir, (2018).** The high- density lipoprotein approved that the effect of supplemented dite with arar leaves a significant increase ($P<0.05$) compared to positive control group. It was proven that there is an increase in HDL. In addition **Vaskonen *et al*. (2002)** indicated that the HDL cholesterol/LDL cholesterol ratio was marginally improved in obese rats due to the fact that arar leaves extract contains phytosterol constituents that enhanced HDL.

On the other hand, the obtained results are consistent with the obtained results by **Abd Elmeged and Alzahrani, (2024)** which proved that arar fruits has a lowering effect on TC, TG, LDL and VLDL. According to **Saswata *et al*., (2013)** the arar communis significantly and dose-dependently decreased lowered TC, TG, LDL, and density VLDL in diabetic rats. This effect may be due to the presence of ascorbic acid in the arar fruits it is beneficial in. Plasma cholesterol levels in hypercholesterolemic humans and animals are typically

significantly reduced when ascorbic acid is added to their diet. This is consistent with **Owu *et al*., (2006)** when its results demonstrated that vitamin C reduced total cholesterol, low-density lipoprotein cholesterol, and plasma triglycerides. As well the obtained result is in line with that of **Saswata *et al*., (2013)** who mentioned that the methanolic extract of arar fruits significantly increased levels of HDL-c.

Obesity and excess weight present a serious risk for the development of renal disorders and chronic kidney diseases. This effect may be attributed to that obesity raises the chance of developing focal and segmental glomerulosclerosis, hypertensive nephron sclerosis, and diabetic nephropathy and it has an impact on the course of stable kidney disease. As well obesity is associated with changes in the structure, histology, and hemodynamics of the kidneys (**Schmidt *et al*., 2015**). Additionally, Obesity has been shown to accelerate the progression of chronic kidney disease (CKD) **(Jung *et al*., 2023).**

The current results indicated that the serum concentrations of BUN, UA and Cr were reduced significantly ($P<0.05$) in obese rats fed on the supplemented HFD with AG and AF or that orally given ALE, compared to obese rats fed HFD alone. Therefore, kidney illness, including chronic kidney disease (CKD), is one of the more subtle effects of obesity (**Prasad *et al*., 2022**). As mentioned by **Wang *et al*., (2015)** there are numerous intricate relationships between obesity and chronic kidney disease (CKD), and the intricacy can be explained by common pathophysiological mechanisms (e.g., hyperinsulinemia, elevated oxidative stress, chronic inflammation, etc.). Insulin resistance, hypertension, dyslipidemia, endothelial dysfunction, sleep disturbances, and other related conditions are among the risk factors and diseases that they share. Furthermore, obesity-related elevated levels of oxidative stress trigger the synthesis of angiotensin-II, which raises plasminogen activator inhibitor-1 and tumor growth factor (TGF) and promotes glomerular fibrosis. The promotion of hypertension in CKD and obesity is facilitated by leptin activation of the sympathetic nervous system, hyperinsulinemia, and native production of angiotensinogen by adipocytes.

The effect of arar gum on lowering serum concentrations of BUN, UA and Cr in obese rats may be related to its fiber content. This is consistent with **Koguchi *et al*., (2004)** who reported that fiber suppresses the elevation of uric acid and urea nitrogen concentrations in serum by attenuating the absorption of dietary adenine.

As well, the evidence indicates that the flavonoid catechin in arar leaves extract may be able to reduce renal damage and alter the disturbance of lipid metabolism. Catechin's antioxidant capacity appeared to be the mechanism underlying its ability to shield the kidney by preventing future membrane damage brought (**Eom *et al*., 2011** and **Chen *et al*., 2011**). These results agreed with **Afolabi *et al*., (2016)** who revealed that catechin dramatically reduced plasma urea and creatinine levels in the treatment groups, even if a complete restoration of renal function was not achieved.

Additionally, the positive effect of arar fruits in the improvement of serum levels of BUN, Cr and UA may be related to its content of flavonoid. As reported by **Banjarnahor and Artanti, (2014)** flavonoids are crucial for treating and preventing renal fibrosis and chronic kidney disease (CKD), according to evidence-based pharmacological studies. By inhibiting or preventing harmful pathways including inflammation and oxidative stress, these substances can both prevent and enhance renal function.

liver disease and obesity are prevalent global health issues that are closely related **(Brunner *et al.*, 2019).**

Since the high effectiveness of liver enzymes (ALT, AST) in the blood is the best indicator of liver damage, their high levels in the blood can be used to predict inflammatory changes in the liver (**Singh and Sharma, 2011**). Hepatic enzymes AST and ALT are the most specific intracellular enzymes that are associated with cell leakage and serve as a marker of hepatocellular injury with greater grades of hepatic steatosis and fibrosis in several studies. The elevation in the hepatic enzymes may be attributed to an increase in the production of free radicals that initiate lipid peroxidation of membrane leading to loss of integrity of cell membranes and damage of hepatic cells. The metabolic processes resulting from a high-fat diet (HFD) can cause oxidative stress in mitochondria and the endoplasmic reticulum, as well as induce de novo lipogenesis and inflammation in liver cells (**Yang *et al.*, 2019**). The results showed that HFD only caused a significant increase in the serum activities of AST, ALT and ALP enzymes in obese rats, compared to that caused by the supplemented HFD with AG and AF or oral administration of ALE in obese rats. The obtained results were in agreement with **Al Shammari, (2020)** who founded that HFD caused significant increase in serum ALT, AST and ALP enzymes as compared to negative control group. Recently, **Huang *et al.*, (2022)** reported the high fat diet significantly elevated the levels of TG, TC, LDL-c, AST, ALT and lowered HDL-c in male mice (**Huang *et al.*, 2022**).

Natural polyphenols are a significant class of phytochemicals that are gaining interest as possible preventative and therapeutic agents for liver disorders. Polyphenols are being considered for liver disease treatments because of their remarkable abilities to reduce inflammation, oxidative stress, lipid metabolism, and insulin resistance. Numerous polyphenols found in a variety of foods and herbs have been shown to treat liver damage through intricate processes (**Li *et al.*, 2018**). The serum levels of AST, ALT and ALP of obese rats fed on the supplemented HFD with arar gum approved that the effect of supplemented diet with arar gum had a significant decrease ($P<0.05$) compared to obese control group. This results may be due to that the arar gum has polyphenols as active component which improve liver functions. This results agreed with **Li et al., (2018)** who proved that polyphenols may prevent injury in hepatocytes. One frequent pathogenetic mechanism that contributes to the development and advancement of hepatic damage in a range of liver illnesses is oxidative stress. When there is a shortage of antioxidant molecules or an excess of reactive species produced from oxygen and nitrogen, cell damage results. Antioxidants

are a sensible therapeutic approach for the management of chronic liver disease based on these data. In certain of these diseases (**Medina and Moreno-Otero, 2005**). Antioxidants are thought to prevent or treat diseases linked to oxidative stress by counteracting the negative effects (**Firuzi *et al*., 2011**). In addition the obtained result is in a consistent with the results of **Al-Attar *et al*., (2020)** that proved that under the influence of arar leaves, the indicators of the biomarkers of liver (ALT, AST, ALP) improved. The antioxidant activity of arar leaves extract (JPLE) was thought to be responsible for its hepatoprotective effects. Therefore implies that arar leaves antioxidant qualities make it a helpful preventative agent. Furthermore, catechin may help improve liver dysfunction. Therefore, catechin extract's ability to reduce these enzymes' activity in mice is proof that it can prevent tissue and cellular damage (**Ravikumar *et al*., 2010**).Catechin's antioxidant activity may be the basis for its capacity to shield the liver from harm, as it might have stopped induced lipid peroxidation from getting worse (**Ved *et al*., 2017).** As well the arar fruit has flavonoids as active component which improve liver functions because Flavonoids have been shown to have positive benefits against and associated illnesses. Numerous defense systems have been discovered. Flavonoids increase the liver's oxidation of fatty acids, which prevents hepatosteatosis **(Akhlaghi, 2016).** Also, arar fruits contains ascorbic acid, which have a hepatoprotective action in mice **(Azhar and Ayub, 2013).**Because of its hepatoprotective properties, ascorbic acid may be used to treat liver injurythat can scavenge and oxidize free radicals, which lowers the stress that toxicants produce in the body and helps to repair the harm that toxicants cause **(Okwulu *et al*., 2021).**

The present study provides a perfect correlation between serum lipid peroxidation products as indicator by MDA and the activity of antioxidant enzymes, which play an important role in the antioxidant system. It showed that fed obes rats on HFD induced significant increase of serum MDA level, and decrease activities of GPx, CAT and SOD enzymes, compared with those of treated obese rats fed on the supplemented HFD with AG, AF powder and oral administration of ALE . The decrease in serum activity of antioxidant enzymes, as seen in serum of obese rats, can lead to the excessive availability of superoxide and peroxyl radicals, which in turn generate hydroxyl radicals, resulting in the initiation and propagation of more lipid peroxidation products. High-fat diets result in the release of free fatty acids by the action of lipoprotein lipase with increase serum triglycerides and cause lipotoxicity, which results in insulin receptor dysfunction. The release of excessive free fatty acids provokes lipotoxicity, as lipids and their metabolites create oxidative stress (**Zhang *et al*., 2007**). The present result was agreed with **Amirkhizi *et al*., (2007)** who showed that increase the production of reactive oxygen species as well as reduced antioxidant defense mechanisms have been suggested to play a role in both humans and animal models of obesity. Further, lipid alterations have been considered as contributory factors to oxidative stress in obesity (**Leopold and Loscalzo, 2008**). Hypertriglyceridemia results in obese rats participate in the alteration of oxidant-antioxidant balance, suggesting increase the bioavailability

of free fatty acids and lipid peroxidation **Amirkhizi *et al*., (2007)**. Hyperlipidemia induces oxidative stress and increase lipid peroxidation (**Moussa, 2008**). Recently, **Denisenko and Novgorodtseva (2013)** showed that fed animals on high fat diet inhibits activity of blood antioxidant enzymes and elevate lipid peroxidation (MDA).

The antioxidant properties arar gum may be due to the presence of dietary fibers in the gum, and this is in consistent with **Thampi *et al*., (1991)** who proved that fibers Impact of fiber on lipid and lipid peroxide levels in rats. The levels of conjugated dienes and MDA were considerably reduced in the gut and liver. It was discovered that SOD and catalase activity had increased. As well, catechins in arar leaves can also significantly improve lipid peroxidation and therefore, treat oxidative stress-induced problems of lipid metabolism (**Zeng *et al*., 2021**). This finding is in consistent with the results of **Alkhedaide *et al*., (2019)** who proved that rats given arar leaves extract showed a significant recovery in the activity of GPx and SOD in liver tissues. The most important potential is the antioxidant activity, which is directly related with the presence of phytochemical compounds in leaves (**Herzi *et al*., 2013**). The effect of arar fruits may be due to its the natural abundance of antioxidant polyphenols that appear to inhibit lipid peroxidation and its high fiber concentration may be responsible for this effect. The lipidemic profile was improved and lipid peroxidation was decreased upon fiber use, indicating that fiber may help lower risk. And verified that the oil present in arar fruits had the potential to prevent oxidation by boosting the activity of GPx, CAT, and SOD (**Höferl *et al*., 2014**).

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هل لنبات العرعر تأثير بيولوجي وهيستوباثولوجي مفيد على الفئران البدينة؟

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قسم التغذية وعلوم الاطعمة – كلية الاقتصاد المنزلي جامعة حلوان

الملخص العربي

يعد استخدام الأعشاب أو النباتات الطبيعية للتحكم في البدانة أو في وزن الجسم أمرًا مثير للاهتمام. لذلك صممت هذه الدراسة لدراسة فعالية الصمغ المستخلص المائي لاوراق وثمار نبات العرعر على الفئران المصابة بالبدانة. أجريت التجربة على ٢٨ فارا ذكرا بالغا من فئران الألبينو المصابة بالبدانة و التي تم تقسيمها عشوائياً إلى ٤ مجموعات (يحتوي كل منها علي ٧ فئران). حيث تم إستخدام المجموعة الأولى كفئران مصابة بالبدانة ضابطة تتغذى على نظام غذائي عالي الدهون فقط، بينما تم تغذية المجموعات الثلاث الأخرى على نظام غذائي عالي الدهون والمضاف اليه صمغ العرعر بنسبة١٠٪ من النظام الغذائي و إعطاء المستخلص المائي لاوراق العرعرعن طريق الفم (١ مل / ١٠٠ جم من وزن الجسم) و المضاف إليه ثمار العرعر بنسبة١٠٪ من النظام الغذائي على التوالي. أظهرت النتائج التي تم الحصول عليها أن الفئران الضابطة البدينة لديها زيادة معنوية ($P<0.05$) في وزن الجسم وكمية الغذاء المستهلكة وكفاءة التمثيل الغذائي وزن الدهون الحشوية ومؤشر السمنة ومستوي الجلوكوزفي الدم ومستوي السيرم من الأنسولين والليبتين و الكوليستيرول الكلي و الدهون الثلاثية و الدهون الكليه و الليبوبروتين منخفض الكثافة و الليبوبروتين منخفض الكثافة جدا و حمض اليوريك و الكرياتينين ونيتروجين يوريا الدم و المالونديالدهيد ونشاط إنزيمات الكبد مقارنة بالفئران البدينة التي تغذت على نظام غذائي عالي الدهون والمضاف اليه صمغ العرعر بنسبة١٠٪ من النظام الغذائي أو إعطاء المستخلص المائي لاوراق العرعرعن طريق الفم (١ مل / ١٠٠ جم من وزن الجسم) او المضاف إلية ثمار العرعر بنسبة١٠٪ من النظام الغذائي على التوالي. كمأ أظهرت النتائج ان افضل تأثير في خفض وزن الجسم وزن الدهون الحشوية، ومؤشر البدانة ومستوي الجلوكوزفي الدم ومستوي السيرم من الأنسولين والليبتن ودهون الدم و حمض اليوريك و الكرياتينين ونيتروجين يوريا الدم كان لدي مجموعات الفئران البدينة المعالجه باستخدام صمغ العرعر و ثمار العرعر والمستخلص المائي لاوراق العرعر علي التوالي. بينما كانت النتائج الافضل في تحسن نشاط إنزيمات ألانين أمينو ترانسفيريز و اسبارتات امينو ترانسفريز الالكين فوسفاتيز ونشاط الانزيمات مضادة للأكسدة و مستوي المالونديالدهيد في السيرم كان في المجموعات البدينة المعالجة باستخدام المستخلص مائي لاوراق العرعر يليه ثمرة العرعر و صمغ العرعر، على التوالي. أظهر الفحص المجهري لمقاطع كبد الفئران البدينة الضابطة وجود دهون في المقاطع المفحوصة وتسللًا للخلايا الالتهابية البابية في الجيوب الكبدية وتدهور واضح في النسيج الكبدي .بينما ظهرت نسبة تسلل أقل للخلايا الالتهابية في مقاطع الكبد لدي الفئران السمينة المعالجة بالنظام الغذائي عالي الدهون المضاف الية صمغ وثمار العرعر. كما ظهر نسبة اقل من الخلايا الالتهابية أحادية النواة العشوائية مع تدهور طفيف للنسيج الكبدي في الفئران البدينة المعالجه بالمستخلص المائي لاوراق العرعر. اظهر الفحص المجهري لمقاطع كلى الفئران البدينة الضابطة وجود تسلل للخلايا الالتهابية حول الأوعية الدموية وانحلال فجوي في الأنابيب الكلوية و في القشرة الكلوية .في الوقت نفسه أظهرت في مقاطع كلية للفئران البدينة المعالجة بصمغ العرعر أنابيب كلوية طبيعية مع التهاب كلوي خلالي بؤري خفيف .بينما ظهر في مقاطع الكلية للفئران البدينة المعالجة بـالمستخلص المائي و ثمار العرعر عن فرط فجوي في أنسجة الكلى ووذمة حول الأوعية الدموية مع تسلل أقل للخلايا الالتهابية. وفي النهاية، لخصت الدراسة إلى أن تناول صمغ او المستخلص المائي للأوراق او ثمار العرعر بشكل منتظم خاصة لمن يعانون من البدانة أو زيادة الوزن له العديد من الفوائد في تقليل الآثار الضارة للبدانة.

الكلمات المفتاحية: البدانة، نبات العرعر، وظائف الكبد والكلى،الإنزيمات المضادة للأكسدة.