Research Article

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Estimation of the Efficacy of Oral Administration of Egyptian *Artemisia herba-alba* Extract in Combating Thyroid Dysfunction in Diabetic Male Rats

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Abstract: Herbal treatments occupy a wide range of medical attempts to treat diabetes, and among these is *Artemisia herba-alba* (AHA) has impressive botanical vegetation in Egypt. For a long time, *Artemisia herba-alba* has been used in traditional medicine as a tonic, diuretic, anthelmintic, and depurative as a result of the occurrence of numerous phytochemical components, such as phenols and flavonoids. Thus, the current study aims to estimate of thyroid efficacy of oral administration of Egyptian AHA. For this purpose, 45 albino rats (male) were distributed into three groups (fifteen rats per group), group 1; control group, group 2; diabetic, group 3; protective group. Subsequently, thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxin-binding globulin (T4) were investigated. Moreover, total flavonoid content (TFC) and total phenolic content (TPC), qualitative screening analyses, and Gas chromatography-mass spectroscopy (GC-MS) were performed. Biochemical investigations, the results showed a slight improvement of T3 in group 3 compared to group 2, while TSH and T4 of group 3 showed an improvement compared to group 2. Furthermore, the qualitative analyses of AHA extract showed the occurrence of flavonoids, alkaloids, reducing sugar, saponins, and tannins. However, the quantitative analyses revealed TPC and TFC values to be 444.15, 8.18, mg GA/g DW, and mg QE/g DW, respectively. GC-MS exhibited the existence of varied bioactive compounds, while the main chemical constituents were Undecane (5.86%), Hexane, 2,5-dimethoxy-2,5-dimethyl (7.32%), trans-Arbusculone (8.54%), (2β,3β,5β)- 2,3,14-trihydroxy-7-ene-6,17-dione, Androst-(8.81%), 4β-Methylandrostane2,3-diol-1,17-dione (5.78%). In conclusion, our results suggested a potent protective effect of *Artemisia herba-alba*, which may be considered as anti-inflammatory agent.
Keywords: *Artemisia herba-alba*; diabetes mellitus; thyroid; qualitative analyses; total phenolic and flavonoid contents; GC-MS.

1. Introduction

Diabetes mellitus (DM) is a medical condition that causes high levels of blood glucose [1]. Long-term, unmanaged diabetes can lead to some organ failure, including the cardiovascular, renal, and central nervous systems [2]. DM is a condition brought on by a genetic defect, an acquired shortage of insulin generated by the pancreas, or the inefficiency of the insulin that is produced. Diabetes-related chronic hyperglycemia results in glycation of body proteins, which has a knock-on effect on the kidneys, thyroid, eyes, arteries, and nerves [3]. In the domains of endocrinology and metabolism, thyroid disorders and diabetes mellitus are both extremely prevalent. Diabetes mellitus and thyroid conditions are frequently found together. Thyroid dysfunction (TD) is widespread among people with type 1 and 2 diabetes than in non-diabetics, according to reports. The link between thyroid health and type 2 diabetes or glucose intolerance is more complicated. Hypothyroidism and hyperthyroidism can both increase the likelihood of developing glucose intolerance [4, 5]. The medical system continues to struggle with effectively managing diabetes without any adverse effects [6]. Reactive oxygen species (ROS) are produced more often and the pancreatic beta-cells ability to undergo apoptosis is activated when blood glucose levels are increased in people with diabetes [7]. The onset of diabetic problems and the induction of renal damage [8, 9]. The pathogenesis of diabetic nephropathy and oxidative stress are closely related [10, 11]. Numerous medical herbs have been suggested for the treatment of diabetes in addition to the current therapy options. Herbs used for traditional medicine are used globally. Due to its efficiency, minimal negative side effects, and inexpensive price, herbal medications are frequently recommended [12]. The amazing botanical vegetation of Egypt includes the *Artemisia herba-alba*, which occupies a wide area among the uses of folk medicine. The volatile oils of *Artemisia herba-alba* have been used a long time ago as a tonic, vermifuge, diuretic, anthelmintic, and depurative. The plant is used to cure exterior wounds and gastrointestinal disorders like diarrhea and cramping [13]. Marrif et al. (1995) stated that *Artemisia herba-alba* is useful in treating jaundice, diabetes, and other illnesses [14]. Furthermore, the ethanolic extract from this species demonstrated activity in the GABAA-benzodiazepine receptor assay, and it was also suggested for neurological illnesses [15]. AHA aqueous extract has been shown in recent studies to preserve the kidneys of streptozotocin (STZ)-induced diabetic

rats [16] and to have long-lasting protective effects [17]. Therefore, the current study aims to evaluate the efficacy of oral administration of Egyptian *Artemisia herba alba* extract in combating thyroid dysfunction in diabetic male rats.

2. Materials and methods

2.1. Chemicals and apparatus

Streptozotocin was obtained from Biovision. Aluminum trichloride anhydrous ($AlCl_3$) was purchased from a High Purity Laboratory Chemicals company (HPLC) (Gujarat, India). The Folin–Ciocalteu reagent (FCR) was purchased from El-Molok for chemicals (Cairo, Egypt), gallic acid (GA) was obtained from the company of Sigma-Aldrich (St. Louis, MO, USA), while the quercetin was purchased from NAWAH Research Center (Cairo, Egypt). TSH, T3, and T4 tests were evaluated by the enzyme-linked immunosorbent assay (ELISA) from Tecan (Männedorf, Switzerland). The TPC and TFC assays were performed using a spectrophotometer from UviLine 9400 (Mainz, Germany). The identification of chemical components of AHA extract was achieved by GC-TSQ Mass-Spectrometer type (Thermo Scientific, Austin, TX) from (USA).

2. Phytochemical analysis

2.1. Qualitative screening analyses

2.1.1. Test for tannins

A (4) mL distilled water was added to 0.1 g of AHA extract boiled in a test tube, and then filtered. Well along, a few droplets of $FeCl_3$ (0.1%, *m/v*) were added, while turning the color to brownish-green or blue-black as indicated by the occurrence of tannins [18].

2.1.2. Test for saponins

A 10 mL of boiling distilled H_2O was added to AHA extract (0.5 g) and then filtered. The mixture was forcefully agitated until forming foam. Three drops of saturated oil were added to the foam, which was then forcefully shaken once more. The formed emulsion proves the occurrence of saponins [18].

2.1.3. Test for flavonoids

The aqueous AHA extract was combined with 3 mL of diluted ammonia. Later, 1 mL of concentrated sulfuric acid (H_2SO_4) was added. Notice the yellow color refers to the occurrence of flavonoids [19, 20].

2.1.4. Test for terpenoids (Salkowski test)

A 3 mL of AHA extract solution was mixed with 1 mL of $CHCl_3$ and 1 mL of conc. H_2SO_4. Notice formation of red-brown coloration revealed the presence of terpenoids [18].

2. 1.5. Test for reducing sugars (Fehling's test)

AHA extract (200 mg) was dissolved in 1 mL ethanol, followed by the addition of 3 mL distilled H_2O. A test tube containing one milliliter of Fehling's solutions A and B was heated to boiling before being mixed with the AHA solution. The existence of reducing sugars was achieved by changing the solution color to red [21].

2.1.6. Test for alkaloids

A 100 mg of AHA extract was added to 2 mL hexane, agitated vigorously, and then filtered. A 3 mL of HCl (2%, *v/v*) was then added to the previous solution. Subsequently, the mixture was boiled, and filtered. Finally, picric acid was added to the solution, the appearance of the yellow precipitate suggests the presence of alkaloids [19, 20]

2.2. Quantitative analyses

2.2.1. Total phenolic contents (TPC) estimation

The Folin & Ciocalteu's reagent (FCR) and an alkaline medium were utilized to estimate the total phenolic content of AHA as described in [22]. Concisely, 1000 µL of FCR was combined with 200 µL of different concentrations of gallic acid as standard (25, 50, 75, or 100 µg/mL) or diluted AHA The mixture was kept standing for 5 minutes. An 800 µL (4%, *m/v*) of Na_2CO_3 sodium carbonate was then added to the reaction medium. For 30 minutes, the mixed solution was left in the darkness and at room temperature. Finally, a spectrophotometer was set to 760 nm to record the solution's absorbance. The sample and standard were analyzed in triplicate. The TPC values are expressed as mg gallic acid equivalent per g of extract on a dry weight basis (mg GA/g DW) by using the calibration curve of GA, where the equation was y= 0.006x–0.01, and R^2= 0.9817.

2.2.2. Total flavonoid content (TFC) estimation

The TFC of AHA was measured as described in [23]. Briefly, 1 mL diluted sample or quercetin standard solution (5-25 µg/mL) was added to a glass test tube, followed by adding 1 mL $AlCl_3$ (2%, *m/v*) solution in methanol. The solution was mixed for 30 sec on a vortex. Leave the mixture to stand at room temperature, then measure at absorbance 430 nm versus methanol as blank after 15 min of incubation. The TFC of AHA extract was expressed as mg quercetin equivalents (QE)/g of extract on a dry weight basis (mg QE per g DW). Calibration curve of the quercetin with equation equal to y= 0.2884x–0.3563, and R^2= 0.9263. The experiments for standard and sample were performed in triplicates.

2.3. Gas Chromatography-Mass Spectrometry (GC-MS) analysis

The tentative characterization of bioactive substances in AHA extract was estimated by using a trace (GC-TSQ Mass Spectrometer) and a direct capillary column (TG-5MS) with (30 m x 0.25 mm x 0.25 µm film thicknesses). The temperature of the column oven was held initially at 50°C and increased by 5°C/min up to 250°C, then held for two minutes, and then increased to 300°C (final temperature) by 30°C per minute held for two minutes. We kept the injector and the temperature of the MS transfer line at 270°C, and 260°C, respectively. Helium was the carrier gas at a flow of 1 mL per min “constant”. The solvent retard was four minutes, and the injection of the diluted sample was 1 mL, and all were automatically by autosampler fixed with Gas Chromatography in the split mode. “MS” the mass spectra at ionization voltages equal to 70 eV above the variety of m/z 50 to 500 in the full scan mode were recorded. 200°C is the temperature of the ion source. Lastly, the chemical components were tentatively identified by the corresponding”MS” in the WILEY 09 library, and NIST 14 mass spectra databases.

2.4. Animal experimental model

From the Animal House (located in the Faculty of Science at Sohag University in Sohag, Egypt) we procured 45 adult male rats (albino), and the weight of the rats was (201±10 g). The animals were prepared for the studies a week before starting. In a habitat with controlled illumination (half-day cycle, lights rise in the morning) and temperature (25±1°C), all animals were housed in 3 cages, each holding 15 animals. Using a random technique. Group (1) was taken care of as a control group and received saline (0.9%), group (2) was set as a diabetic group, which injected intraperitoneally (IP) with STZ (single dose, 50 mg /kg body weight) for fifteen days, while the final group (3) was set as a protective group and received *Artemisia* extract (50 mg /kg body weight) before receiving of STZ (single dosage, 50 mg per kg body weight). This work was accomplished according to Sohag University animal guidelines and approved by the ethical committee approval number (CSRE-19-23).

2.5. Induction of diabetes

The IP injection of a single dosage of 50 mg per kg of body weight of STZ [a fresh solution of streptozotocin was prepared with citrate buffer with 0.1 M and pH 4.5], was utilized to diabetes induction [24]. After 72 hrs, rats with blood glucose (FBG) levels above 200 mg/dl were well-thought-out as diabetic rats.

2.6. Blood sampling

The experiment was terminated after fifteen days, and the blood samples from the artery were gathered and placed in sample tubes for analysis. Later, a centrifugation at 3000 rpm for 10 minutes was carried out to obtain the serum, and then was transferred to an Eppendorf, and kept at -20°C for further biochemical investigations.

2.7. Biochemical analysis estimations

Serum TSH, T3, and T4 were estimated by suitable ELISA kits. All tests were examined according to the manufacturer's instructions and procedures of Biovision Company.

2.8. Statistical analysis

Thyroid markers were expressed by mean values with standard deviation way (M ± SD). Subsequently, data were analyzed by (ANOVA), followed by the Newman-Keuls test. The GraphPad Prism® Software program version five from (SanDiego, CA) was used for the statistical analysis, while $p < 0.05$ was regarded to be statistical significance.

3. Results and Discussion:

3.1. phytochemical analysis:

3.1.1. Qualitative screening analyses:

The findings of the phytochemical screening analysis of AHA extract revealed the occurrence of numerous phytochemicals, such as saponins, alkaloids, flavonoids, tannins, and reducing sugars (**Table 1**). Our results matched with another study performed by Ahmed et al. (2020) [25]. Furthermore, the previous study [18] mentioned that the plant has valuable components, which will make it highly recommended for medical treatment.

Table 1: Phytochemical screening analysis of *Artemisia herba-alba* extract.

No	Phytoconstituents	Test	Result
1	Tannins	---	+
2	Saponins	Froth	+
3	Flavonoids	----	+
4	Reducing sugars	Fehling's	+
5	Terpenoids	Salkowski	-
6	Alkaloids	----	+

3.1.2. Total phenolic and flavonoid contents:

The assessment of total phenolic and flavonoid contents of *Artemisia herba-alba* was performed using the Folin-Ciocalteu and aluminum chloride reagents, respectively. The result of TPC (**Table 2**) displayed that the *Artemisia herba-alba* contains higher contents of phenols, which may be highly recommended in medical treatment. The TPC value of AHA was 444.15 (mg GA/g DW), while the TFC was 8.81 (mg QE/g DW). Comparison of our results with other published papers revealed different and varied total phenolic/flavonoid contents. For instance, in Tunisia, TPC value was 8.38 ± 0.75 (mg GA/g DW), and the TFC was 16.15 ± 1.44 (mg QE/g DW) [26], in Saudi Arabia, TPC was 94.19 (mg GA/g DW) [27], and the value of TFC was 99.7 (mg QE/g DW) [28], however, in Algeria, TPC was 514 (mg Tannic Acid/g DW), and the value of TFC was 10.61 (mg QE/g DW) [29].

Table 2: Estimation of total phenolic and flavonoid contents of *Artemisia herba-alba* extract (Values represent mean ± SD).

Sample	TPC (mg GA/ g DW)	TFC (mg QE/g DW)
AHA	444.15 ± 2.2	8.81 ± 0.02

3.1.3. GC-MS analysis:

The bioactive substances of the Egyptian *Artemisia* extract were tentatively identified using GC-MS. The results of this analysis were summarized in (**Table 3**), the total ion chromatogram (TIC) was presented in **Fig. 1**, and the identified compounds in **Fig. 2**. The data exhibited various phytochemical constituents, however, the major compounds were 13,16-Octa-deca-diynoic acid, methyl ester **(1)**, Undecane **(2)**, Hexane, 2,5-dimethoxy-2,5-dimethyl **(3)**, cis-Vaccenic acid **(4)**, 13-Oxabicyclo[10.1.0]tri-decane **(5)**, trans-Arbusculone **(6)**, Bi-cyclo [4.3.0] nonan-4-one,9-(2-methoxy-ethoxy-methoxy)-1-methyl-**(7)**, Methyl-2- hydroxy-4-methoxy-benzoate **(8)**, Dodecane **(9)**, 3-(5-Methyl-5-vinyl-tetra-hydrofuran-2-yl) butan-2-ol **(10)**, 2,2-dimethyl-5-(3-methyl-2-Oxiranyl) cyclo-

hexanone **(11)**, Davana ether- **(12)**, 9,12-Octadecadienoic acid **(13)**, (S,E)-6-Hydroxy-6-methyl-2-((2S,5R)-5-methyl-5-vinyl-tetra-hydrofuran-2-yl)-hept-4-en-3-one **(14)**, Androst-7-ene-6,17-dione,2,3,14-trihydroxy-, (2β,3β,5β)- **(15)**, 4β-Methyl-androstane2,3-diol-1,17-dione **(16)**.

Among the identified compounds we found, many valuable and influential compounds that participate in the value of AHA and support its effect, such as 13-Oxabicyclo tri-decane are found to be used in drug manufacturing for breast cancer according to Thambidurai [30]. Tricyclo [20.8.0.0(7, 16)] tri-acontane, 1(22),7(16)-diepoxy- was determined to be potential novel anti-diabetic drugs [31]. Also, Androst-7-ene-6, 17-dione, 2,3,14-trihydroxy-, (2β,3β,5β) is a hypolipidemic agent [32]. Methyl-2-hydroxy-4-methoxybenzoate is frequently used in enantioselective synthesis by bioactive natural products involving two components [33]. Furthermore, we found Undecane, which is an antibacterial agent, while cis-Vaccenic acid has an antibacterial activity and hypolipidemic effect in rats. In addition, 9,12-Octadecadienoic acid has been used widely in the pharmacological industry, such as cancer preventive, anti-inflammatory, anti-acne, antihistaminic, anti-eczema. 13, while 16-Octadecadienoic acid, is methyl ester, which is anti-inflammatory, antioxidant, and antimicrobial [34].

Table 3: Estimation of total phenolic and flavonoid contents of *Artemisia herba-alba* extract.

No.	R.T.	Area (%)	Compound name	Molecular formula	M.wt
1	4.11	1.56	13,16-Octadecadiynoic acid, methyl ester	$C_{19}H_{30}O_2$	290
2	4.39	5.86	Undecane	$C_{11}H_{24}$	156
3	4.68	7.32	Hexane, 2,5-dimethoxy-2,5-dimethyl	$C_{10}H_{22}O_2$	174
4	5.11	2.36	cis-Vaccenic acid	$C_{18}H_{34}O_2$	282
5	5.40	2.36	13-Oxabicyclo[10.1.0]tri-decane	$C_{12}H_{22}O$	182
6	6.92	8.54	trans-Arbusculone	$C_9H_{14}O_2$	154
7	10.29	1.91	Bi-cyclo [4.3.0] nonan-4-one,9-(2-methoxy-ethoxy-methoxy)-1-methyl-	$C_{14}H_{24}O_4$	256
8	11.31	3.78	Methyl-2-hydroxy-4-methoxybenzoate	$C_9H_{10}O_4$	182
9	11.94	1.27	Dodecane	$C_{12}H_{26}$	170
10	14.84	2.03	3-(5-Methyl-5-vinyltetrahydrofuran-2-yl)butan-2-ol	$C_{11}H_{20}O_2$	184
11	15.51	2.92	2,2-dimethyl-5-(3-methyl-2-Oxiranyl)cyclo-hexanone	$C_{11}H_{18}O_2$	182
12	16.64	1.86	Davana ether-	$C_{15}H_{22}O_2$	234
13	19.43	1.40	9,12-Octadecadienoic acid	$C_{19}H_{34}O_2$	294
14	21.18	5.87	(S,E)-6-Hydroxy-6-methyl-2-((2S,5R)-5-methyl-5-vinyltetrahydrofuran-2-yl)-hept-4-en-3-one	$C_{15}H_{24}O_3$	252
15	35.45	8.81	Androst-7-ene-6,17-dione,2,3,14-trihydroxy-, (2β,3β,5β)-	$C_{19}H_{26}O_5$	334
16	35.78	5.78	4β-Methylandrostane2,3-diol-1,17-dione	$C_{20}H_{30}O_4$	334

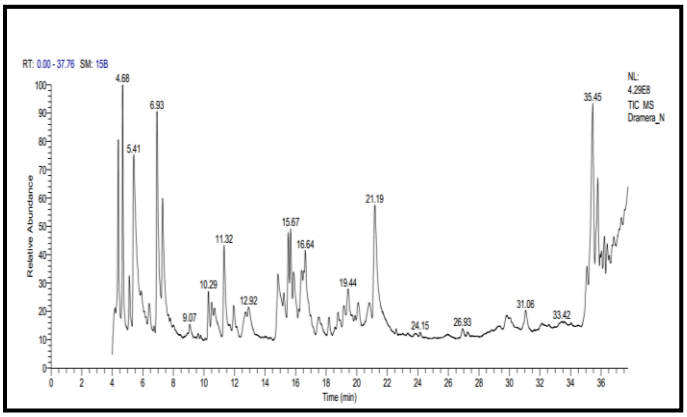
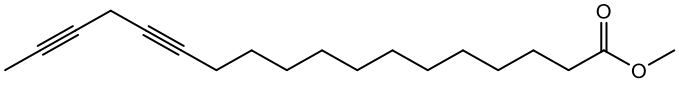
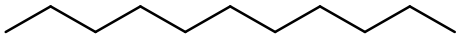


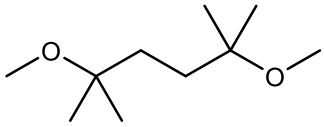
Fig. 1: Total ion chromatogram of GC-MS analysis of *Artemisia herba-alba* extract.



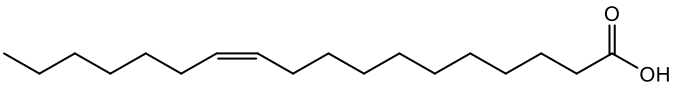
13,16-Octadecadiynoic acid, methyl ester **(1)**



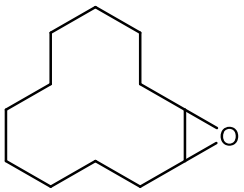
Undecane **(2)**



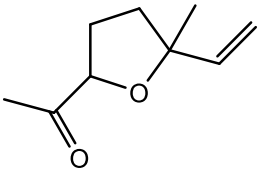
Hexane, 2,5-dimethoxy-2,5-dimethyl **(3)**



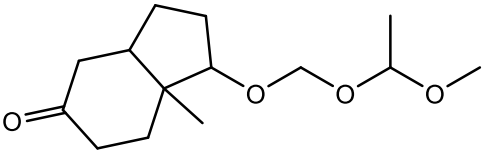
cis-Vaccenic acid **(4)**



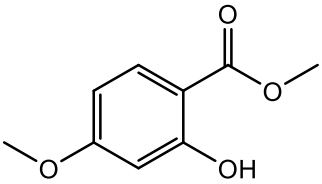
13-Oxabicyclo [10.1.0] tri-decane **(5)**



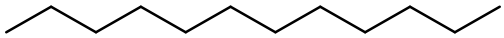
trans-Arbusculone **(6)**



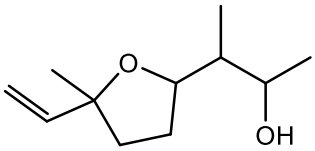
Bi-cyclo [4.3.0] nonan-4-one, 9-(methoxyethoxymethoxy)-1-methyl- **(7)**



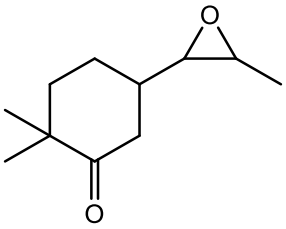
Methyl-2-hydroxy-4-methoxybenzoate **(8)**



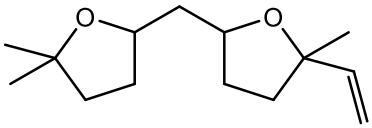
Dodecane **(9)**



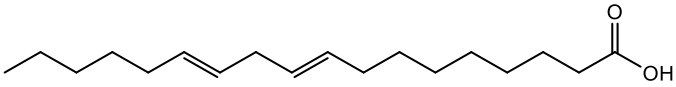
3-(5-Methyl-5-vinyltetrahydrofuran-2-yl) butan-2-ol **(10)**



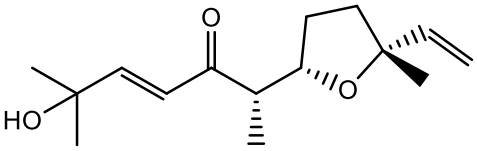
2,2-Dimethyl-5-(3-methyl-2-oxiranyl) cyclo-hexanone **(11)**



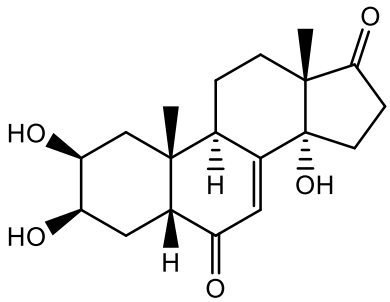
Davana ether- **(12)**



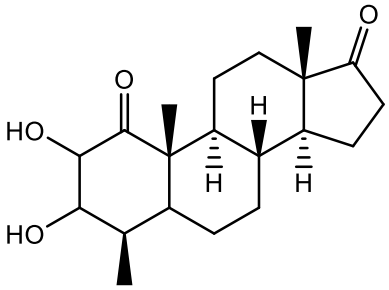
9,12-Octadecadienoic acid **(13)**



(S,E)-6-Hydroxy-6-methyl-2-((2S,5R)-5-methyl-5-vinyltetrahydrofuran-2-yl)-hept-4-en-3-one **(14)**



Androst-7-ene-6,17-dione,2,3,14-trihydroxy-, (2β,3β,5β)- **(15)**



4β-Methylandrostane2,3-diol-1,17-dione **(16)**

Fig. 2: Chemical structures of identified compounds of *Artemisia herba alba* extract using GC-MS.

3.2 Biochemical analysis:

Hyperglycemia is a characteristic of the metabolic illness known as diabetes mellitus. Diabetes mellitus is linked to macrovascular and microvascular problems [35] in addition to hyperglycemia. AHA has been used widely to cure numerous diseases, in addition to diabetes, in Moroccan and Iraqi folk medicine [36, 37]. In our study, the estimation of the efficacy of administration of *Artemisia* extract (orally) was evaluated using thyroid markers, including TSH, T3, and T4. Taken into consideration one of the signs of diabetes has long been acknowledged to be weight loss [38].

In our previous work [39], we investigated the effect of AHA on blood sugar levels and body weight change of rats during the study period. in the results revealed the extract's ability to reduce blood Glucose levels, and to improve body weight. Therefore, the hypoglycemic effect of AHA extract paves the way for studying the AHA extract further on various vital functions of the body, including the thyroid gland, kidneys, liver, etc.

3.2.1. Thyroid function:

The thyroid gland disorder is no less important than other interactions resulting from diabetes. One of the functions of the thyroid gland is the regulation of metabolism and energy equilibrium [40]. The dysfunction of the thyroid affects the muscle increases insulin resistance [41] and reduces glucose transportation [42]. The basic function of thyroid hormone is stimulating the basal expressions of glucose transporters, to control the consumption of intracellular glucose on myocytes surface [43, 44]. Diabetes mellitus is a systemic disease; in many cases, people with diabetes also have thyroid dysfunction. In the field of endocrinology and metabolism, DM and thyroid disorders are both highly prevalent. [45]. Patients that have type 2 diabetes mellitus (T2DM) are more susceptible than non-diabetic patients to developing both hypothyroidism and hyperthyroidism [46]. A previous study [47] illustrated that among the patients studied that have diabetes, they found 69 % of patients had a full normal thyroid profile, while 31 % had thyroid dysfunction divided into 25 % were sub-clinical hypothyroidism also there 3.5 % were hypothyroidism, finally 2.5 % had hyperthyroidism. This previous study illustrated the impact of diabetes on disturbed thyroid function which in turn affects body vitality. Therefore, it's necessary to diagnose thyroid disorder in diabetic patients to prevent further

complications. Our study evaluated the protective effect of AHA extract on the thyroid hormone profile (**Table 4**). The serum levels of T4 decreased in the protective group to be much closer to the negative control and significantly enhanced in the protective group compared to the positive control ($p < 0.05$). Furthermore, T3 level was decreased at the protective group serum level compared with the negative group and positive control group. TSH was increased in the protective group and enhanced to be close to the negative control group ($p < 0.05$). *A. herba-alba* extract results show considered a good antioxidant plant that can help the body to improve its vital balance. All results indicated the *Artemisia herba-alba* extract has a good impact on thyroid function, and it already enhances the thyroid facing the diabetes consequences to the thyroid hormones. Our findings may illustrate more improvement for the thyroid dysfuncation, if we give the protective group (group 3) more time and/or more dosage from *Artemisia herba-alba* extract.

Table 4: Effects of *Artemisia herba-alba* extract on the serum of TSH, T3, and T4.

Groups	Control	Diabetic	Protective
TSH (mIU/mL)	2.10 ± 0.10	1.10 ± 0.09***	2.00 ± 0.04$^{n.s,\#\#\#}$
T3 (mmol/L)	2.03 ± 0.04	2.30 ± 0.10*	1.80 ± 0.10$^{n.s,\#}$
T4 (µg/dL)	6.50 ± 0.10	8.00 ± 0.20***	6.80 ± 0.10$^{n.s,\#\#\#}$

*****, Significant change in comparison between the control group and other groups, where $*p < 0.01$, $***p < 0.001$. **#**, Significant change in comparison between diabetic and protective group, where $^{\#}p < 0.01$, $^{\#\#\#}p < 0.001$. **ns**, non-significant ($p > 0.05$) between the control group and other groups. The significance was performed using One-way ANOVA, followed by the Newman-Keuls test.

4. Conclusion

Artemisia is widely used in variation forms to treat multiple clinical disorders. Our research work attempted to provide evidence for the slight prophylactic action of AHA extract against diabetes mellitus and associated gland problems. Our study strengthens the case for the health benefits of consuming *A. herba-alba* among Arabic people and offers support for more focused applications in drug discovery. The results revealed that oral administration of *A. herba-alba* significantly enhanced thyroid serum levels of T3 and TSH in the protective group near the control. On the other hand, it was discovered that the protective effect of AHA extract on the serum T4 level was close to the control. Additionally, our results showed higher total phenolic contents, which may boost its significance in treating multiple disorders. Several phytochemicals, including phenols and flavonoids, are known to have a wide range of pharmacological effects. GS-MS analysis of the AHA extract revealed the occurrence of different classes of bioactive compounds, which may be the reason for the the protective effect of the plant on the thyroid and may confirm its valuable future therapeutic power. Therefore, some further investigations on the kidney and/or other organs will be required to assess the efficacy of *Artemisia herba alba* as a potential antidiabetic agent. Moreover, the separation, characterization, and action mechanism of bioactive substances in this species will be needed to determine the role of the *A. herba-alba* in diabetes mellitus management.

CRediT authorship contribution statement:

Nagwa Mohamed El-Sawi: Supervision, Conceptualization, Writing–review and editing. *Omar Mohamed El-Hady*: Supervision, Conceptualization, Writing–review and editing. *Amira Hamdy El-Aref*: Investigation, Formal analysis, Data curation, Writing–original draft preparation. *Mahmoud Hefny Gad*: Supervision, Conceptualization, Methodology, Visualization, Data curation, Writing–original draft preparation, Writing–review and editing. All authors have read and agreed to the published version of the manuscript.

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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