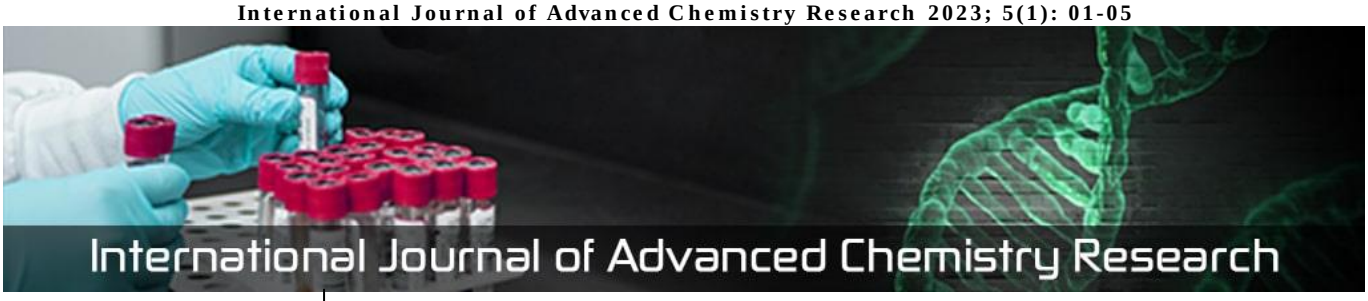

ISSN Print: 2664-6781
ISSN Online: 2664-679X
Impact Factor: RJIF 5.32
IJACR 2023; 5(1): 01-05
www.chemistryjournals.net
Received: 03-10-2022
Accepted: 08-12-2022

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Study of the activity of the adropin hormone and some biochemical variables in patients with diabetic nephropathy in Kirkuk city

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Abstract
The study aimed to show the relation between the level of the Adropin hormone and diabetic nephropathy patients, in addition to measuring the lipid profile, as well as the level of uric acid, creatinine, and urea. Diabetic nephropathy (DN) is the main risk parameter for a diversity of adverse prognosis results because it affects directly the cardiovascular system, particularly, in diabetic nephropathy patients, and so far it has been shown that natural products have a significant impact on preventing the growth of DN. Adropin hormone is a peptide discovered in 2008 by Kumar *et al* which involves 76 amino acids. Adropin is effective in lowering blood sugar and improving insulin resistance. The study included ((60) blood samples for people with diabetic nephropathy and both sexes, their ages ranging between (35-80) years, which were taken from the people who visited Kirkuk Hospital. The outcomes of the work displayed a significant increase in the possibility (0.001 ($P\leq$) level in the hormone adropin and the level of creatinine, urea, and uric acid in the patients with diabetic nephropathy compared to the normal ones. The results also displayed a major increase in the lipid profile (cholesterol, triglycerides, LDL-C, VLDL-C), and a large decrement in the concentration of HDL-C in the group of people with diabetic nephropathy compared with the healthy ones.

Keywords: Adropin hormone, diabetic nephropathy

Introduction
Diabetes is a kind of metabolic illness known because of increased sugar in the blood, which can be divided into two types which are known as type one and type two. Recent research has shown that high glucose levels lead to tissue dysfunction and lead to the emergence of many diseases, including kidney diseases, vascular and nerve diseases, and others. [1, 2]. It is one of the most public metabolic illnesses, which is usually connected with increased blood sugar and poor conversion of carbohydrates, proteins, as well as fats, and the inability to benefit from them [3]. Global, finds that millions of people have this illness, and the statistics have shown that the many patients who suffer from diabetes will reach in 2022 to 300 million patients. [4]. Diabetes causes many complications for affected people, including vascular diseases and heart diseases, as well as vision disorders and sometimes blindness, skin diseases, and sometimes complications that may reach mental disorders. [5]. DN is one of the most popular complications spread among people who suffer from diabetes [6, 7, 8] and 30% of patients were affected and representing a significant public health burden [9]. It is described by continuous albuminuria (albumin secretion >300 mg/hr in 24 hours or >200 mcg/min) or an albumin/creatine ratio >20 with the urine in the morning also accompanies some symptoms like the existence of retinopathy and the lack of present some laboratory which findings that may appear other diseases of renal [10, 11]. Albumin excretion (AE) and glomerular filtration rate (GFR) is the first clinical marker for the detection and initiation of micro albuminuria and DN [10, 12]. While micro albuminuria (primary nephropathy) is an important indicator of albuminuria progression (>300 mg/dL) or nephropathy, these measures are not sufficiently helpful for the revelation of the progression of illness early [13, 14]. Some of the patients, particularly patients who suffer from the second type of diabetes, hypoalbuminemia, and chronic kidney disease report urine albumin incompatibility in monitoring renal nephropathy [13]. This conflict is found in some cases, such as the patients who suffer from micro albuminuria have normal renal function while the patients

who suffer from diabetes with normal albuminuria have renal disorders. [15, 16]. Some research has presented that chronic kidney disease (CKD) is spread by 13.4% in China and this rate is growing every year thus it has become a serious common health concern. [17]. Diabetic nephropathy DN involves a complex pathological mechanism with hyperglycemia, extreme levels of reactive oxygen species (ROS), and reduced autophagy cells. Additionally, DN is a major hazard parameter for a diversity of adverse prognosis results because it directly affects the system of cardiovascular, particularly for patients who suffer from diabetic nephropathy [18, 19]. Since diabetic nephropathy DN is affected by many factors including complex pathological mechanisms, efficient and particular medications for its treatment are currently rare, and so far it has been shown that natural products have a major influence on stopping the growth of DN. Such as salidroside from *Rhodiola Rosea* L. has been stated to mitigate diabetic nephropathy by downregulating the TGF-β1/Smad2/3 pathway [20]. Qi Chi and coworkers set that chromium picolinate can be inverse diabetic nephropathy by preventing oxidative and inflammatory pathways, and it is probable to be permitted utilized as a drug supplement [21]. In addition, cyanidin-3-glucoside from black rice has also been shown to mitigate DN nephropathy by down regulating TGF-β1/Smad2/3 related to the pathway of aggregation extracellular matrix [22, 23]. Between the many normal complexes, flavonoids have prominent influences on drugs, involving anti-inflammatory, ant diabetic, antioxidant, and antihypertensive effects [24, 25, 26]. The flavonoids used by traditional Chinese medicine have proven their effectiveness in treating DN. For example, it was found that baicalin, which was applied to mice with diabetic kidney disease, has a key role in curbing the growth of CKD caused by streptozotocin. Kaempferol has been revealed to reduce the damage of the kidney through its effects of an anti-oxidant and anti-inflammatory. The pathogenesis of DN is complicated and still ambiguous, but the research done so far has displayed that hyperglycemia-induced renal artery hypertension, extreme levels of (ROS) and reduced podocyte autophagy are strictly associated with the incidence of DN. Diabetic kidney DN [27].

Adropin is a harmonic peptide discovered by the scientists Kumar and his colleagues in the year 2008 [28]. Adropin's name comes from the Latin word aduro i.e make fire and pinquis i.e. fats or oils [29]. Adropin contains seventy-six amino acids and it is characterized as a secreted peptide, with remains1–33 encoding the secretory signal sequence of the peptide. And the sequence of amino acids of Adropin is identical in humans, mice, and rats. Recent data indicate that adropin has the function to balance energy and monitoring glucose and fatty acid metabolism [51, 52]. In some of the literature was found that adropin adjusts the expression of genes of hepatic lipogenesis and the PPARã receptor (peroxisome proliferator-activated receptor), a key adjust lipogenesis. Endothelial cell protection [52]. Adropin is encoded by the Enho gene, which is mainly expressed in the liver and central the system of nervous [32, 33, 34, 35]. Adrobin was recently said to be a cell membrane-associated protein, with a high appearance in the brain (6-fold higher compared to the liver). Adrobin as a membrane-associated protein can regulate cellular communication [52]. Furthermore, its expression in the central system of the nervous may indicate that it has neuropeptide properties and Adropin may act as an autocrine /factor on peripheral tissues [36].

Materials and Methods

This work under investigation was done in the laboratories of the General Hospital of Kirkuk and the Public Health Laboratory Governorate Kirkuk from September 2021 to January 2021. The sample of the study is (60) samples who suffer the diabetic nephropathy, among them (32) men and the remaining (28) women, with ages from 35 to 80 years. As well as it was collected (30) blood samples (15 men, and 15 women) from normal people who were selected randomly from the people of governorate Kirkuk. The blood samples were collected in plain tubes with tight-fitting EDTA-free plastic tubes and kept for 15 min at RT until coagulation was then placed in a centrifuge at 3000 rpm for 10 min. The blood serum was taken by micropipette and placed in a test tube, and then kept at -20 °C to the required tests were performed. The lipid profiles (cholesterol, TG, HDL-C, LDL-C, VLDL-C, Adropin hormone, urea, creatine, and uric acid levels) were estimated.

Results and Discussion

The results are shown in Table (1-1) showed a major increment at the level ($p \leq 0.001$) of the hormone adropin in DN patients in comparison with healthy ones. Marked by atropine levels in patients with diabetes mellitus [38], Zang *et al*. [39] showed a decrease in concentrations of serum of adropin in patients of Chinese T2DM, particularly who suffer from overweight/obese. Wu *et al*. [40] recorded a major reduction in serum adrobin level in T2DM patients compared to patients non-diabetic, and showed that reduced serum adrobin was also related to atherosclerosis coronary in T2DM and so far the patients of non-diabetic, While the study of Hu and Chen) [41] showed that blood levels of adrobin were negatively related to kidney function and may be contributing to causing the growth of DN, it found patients with T2DM (type 2 diabetes mellitus) with nephropathy showed lower adrobin levels. Relative to those without CKD However, this suggests that adropin can help as a biomarker to predict the risk of DN and our results were in conflict with those of Hu and Chen)] [41]. Adropin contributes to carbohydrate and lipid metabolism, metabolic disease, and central system nervous function.

Table 1: Mean ± Standard Deviation of the concentration of the hormone Adropin in the sera of diabetic nephropathy patients compared with the healthy controls.

Factor	Control	Patient	P value
Adropin	4.63 ± 2.18	14.72 ± 3.22	0.0007**

** ($p \leq 0.001$)

Table (1-2) displays that there are major variances at the level of probability ($p \leq 0.001$) for the hormone adrobin in both men and women for diabetic nephropathy patients compared with the healthy controls.

Table 2: Levels of adrobin hormone in the sera of diabetic nephropathy patients compared to healthy subjects by gender

Groups Parameter	Mean ±SD			
	Patients (n=60)		Control (n=30)	
	Women (n=28)	Men (n=32)	Women (n=15)	Men (n=15)
Adropin	±3.222 14.589	14.843±3.275	4.520±2.379	4.740±2.034
P-Value	0.00004**		0.00004**	

Lipid profile

The lipid profile was measured in the blood of patients with diabetic nephropathy and comparison with the normal group, as the statistical results displayed in Table (1-3) showed a major increment at the probability level ($p \leq 0.001$) for the level of cholesterol, triglycerides, LDL-C and VLDL-C. And a major reduce at ($p \leq 0.001$) level for the level of HDL-C.

Table 3: Mean ± standard deviation of lipid levels in the sera of diabetic nephropathy patients compared to healthy controls.

Factor	Control (mean ± SD)	Patient (mean ± SD)	P value
Cholesterol	173.7±11.1	240.0±33.9	0.0006**
Triglycerides	110.78±6.25	226.07±6.07	0.00002**
HDL-C	47.79±6.64	84.63±8.23	0.0008**
LDL-C	103.5±28.2	158.3±14.5	0.0005**
VLDL-C	69.0±3.7	208.0±8.1	0.0004**

** ($p \leq 0.001$)

The increase in triglycerides is due to the increase in the intake of foods rich in fats that lead to an increase in the production of chylomicrons in the intestine, which when decomposing causes the release of fatty acids. Therefore, liver cells will receive large amounts of fatty acids, causing an increase in the release of glycerides. Triple in VLDL-C [42].

The increase in both LDL-C and VLDL-C contradicts (ES-HAGHI 20211), as the reason for the increase in LDL-C is due to the breakdown in the binding of LDL-C to receptors in the liver, which shows a major role in reducing the transformation of LDL-C To the hepatic tissues and then increase its concentration in the blood serum, which leads to a rise in the harmful LDL-C cholesterol [43].

Table (1-3) shows a major decrease at ($p \leq 0.01$ level) for HDL-C for the patients with diabetic nephropathy in comparison to healthy groups. The decrement in the activity of the enzyme lipoprotein lipase (LPL), which leads to the degradation of TG to fatty acids and glycerol, and the decreased degradation of VLDL-C molecules leads to the depletion of HDL-C molecules by blocking the transfer of Apo proteins and phosphorylated lipids from TG to HDL-C [45].

Table (1-4) shows that there are significant differences at level ($p \leq 0.001$) for the level of cholesterol, triglycerides, LDL-C, and VLDL-C, and a major decrease at ($p \leq 0.001$) level for the HDL-C level. In both men and women with diabetic nephropathy, comparison with the healthy controls.

Table 4: Levels of lipid profile in the serum patients of diabetic nephropathy compared to healthy subjects by sex

Groups Parameter	Mean ±SD				P-Value
	Patients (n=60)		Control (n=30)		
	Women (n=28)	Men (n=32)	Women (n=15)	Men (n=15)	
Cholesterol	±17.50237.17	±14.49242.47	172.47±9.92	174.87±12.44	0.0008**
Triglycerides	±6.45226.38	±5.82225.79	111.48±6.95	110.07±5.62	0.00006
HDL-C	±7.5485.43	83.93±8.85	47.88±6.31	47.71±7.17	0.00007
LDL-C	±14.35157.31	±14.75159.13	104.05±34.53	102.94±21.25	0.00001
VLDL-C	207.0 ± 7. 1	208.0 ± 8.01	69.0 ± 2.7	67.0 ± 3.9	0.00005

Vital Variables

The biomarker level of uric acid ion, creatinine ion, and urea ion was measured in the blood serum of patients with diabetic nephropathy compared to healthy controls, and the finding is shown in the table, respectively. (1-5).

Table 5: Mean ± standard deviation of the level of Uric Acid in the sera patients with diabetic nephropathy in comparison with the healthy groups.

Parameter	Control mean ± SD))	Patient mean ± SD))	P value
Uric Acid	4.64±1.25	7.10±1.34	0.0004**
Creatinine mg/dl L	14.2±4.40	27.4±21.2	0.0002**
Urea	1.008±0.185	1.386±0.478	0.0003**

The finding displayed a major increment ($p<0.001$) in each of the levels of uric acid, creatinine ion, and urea ion for patients with diabetic nephropathy compared to the control group, respectively.

The high creatinine concentration in the patient's blood of DN may be attributed to the fact that creatinine is a metabolic waste that is naturally excreted through diuresis. Glomerular, a slight decrease in (GFR) leads to an increment in the creatinine concentration in the blood [46]. The work under investigation also indicated the presence of an increase in the level of urea, and the reason may be due to kidney injury, which leads to an increment in the concentration of creatinine in the blood. [47]., the reason for this may be due to the narrowing of the renal artery, which helps in the occurrence of nephrosclerosis, which is diagnosed by the presence of thickness in the small capillary arteries, which leads to high creatinine in patients and occurs as a result of a decline in the glomerular filtration rate (GFR), as well as some Other diseases like as, high blood pressure, and diabetes [48].

Table (1-6) shows that there are significant differences at ($p \leq 0.001$) for the level of uric acid, creatinine ion, and urea ion. In both men and women of DN patients, compared with healthy controls, respectively.

Table 6: levels of uric acid in the sera of diabetic nephropathy patients compared to healthy subjects by sex.

Groups Factor	Mean ±SD			
	Patients (n=60)		Control (n=30)	
	Women (n=28)	Men (n=32)	Women (n=15)	Men (n=15)
Uric acid mg/dl	±1.063 6.196	±1.0357.888	4.527±1.118	4.760±1.396
P-Value	0.0009		0.0009	

Table 7: levels of urea in the sera of diabetic nephropathy patients compared to healthy controls, by sex

Groups Parameter	Mean ±SD			
	Patients (n=60)		Control (n=30)	
	Women (n=28)	Men (n=32)	Women (n=15)	Men (n=15)
Urea mg/dl	25.49±8.94	±7.69 28.78	13.23±4.26	15.21±4.45
P-Value	0.577			

Table 8: creatinine levels in the sera of diabetic nephropathy patients compared to healthy subjects, by gender

Groups Parameter	Mean ±SD			
	Patients (n=60)		Control (n=30)	
	Women (n=28)	Men (n=32)	Women (n=15)	Men (n=15)
Creatinine (mg/dl L)	0.460±1.392	±0.50031.3803	1.0127±0.1509	1.002±0.2213
P-Value	< 0.0001			

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