ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at www.jgpt.co.in

RESEARCH ARTICLE

Effect of Some Types of Doping Used by Athletes on Liver and Kidneys Functional Performance in Albino Male Rats

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Abstract

The studies and researches at the present time interested with doping especially the anabolic androgenic steroids (AAS) due to their commonly used by the athletes and non-athletes , as well as study the effect of these doping on body organs and its tissues such as liver and kidneys, effectiveness of hepatic enzymes, the variations in the performance of liver and kidney functions, in addition to the hepatic pathological changes like cirrhosis, congestion, necrosis, increased collagen content in the liver parenchyma and disturbance in the glomerular filtration process of kidney. Therefore, this study aimed to use Nandrolone decanoate doping (ND) that has been possessed anabolic androgenic ability and diagnosis its influences on the tissues of some organs especially liver and kidneys. The current study was performed in the animal house return to the Biology department / Faculty of Education for Girls / Kufa University, in this study (30) male rats of Sprague-Dawley strain were used and divided into two main groups, the first group was the control group comprised (15) rats were also divided into three equal subgroups, a group was injected with normal saline solution (0.9%) once a week for one month, a group was also included (5) rats injected with (0.9%) normal saline solution one time weekly for two months and the last group was also injected with normal saline (0.9%) once weekly for three months, while the second group was contained (15) rats and divided into three equal subgroups, a group was injected with Nandrolone decanoate doping (ND) at the concentration of (1 mg/kg) once weekly for one month, a group was injected with (1 mg/kg) of (ND) doping also one time at week for two months, concerning to the last group was injected with (ND) doping at the concentration of (1 mg/kg) once a week for the period of three months, the injection process of all treatments was intramuscular (in the hind limb muscle) for each rat. The study was contained, body weight recording as well as the relative weights of liver and kidneys, estimation of some biochemical parameters of the blood as: Aspartate amino transferase (AST), Alanine amino transferase (ALT), Alkaline phosphatase (ALP), the levels of total bilirubin, total protein, albumin, total cholesterol, triglycerides, creatinine and urea, whereas the histological study included, preparation of tissue sections for the liver and kidneys. The statistical analysis of study were revealed : a significant increase ($p<0.05$) in the body weight, relative weights of liver and kidneys, effectiveness of hepatic enzymes (AST, ALT, ALP), levels of total bilirubin, total protein, albumin, total cholesterol, triglycerides, creatinine an urea at the groups were treated with Nandrolone decanoate doping compared to the control groups . With regard to the microscopic examination of liver and kidneys sections for male rats that injected with Nandrolone decanoate doping were exhibited various patho-histological changes when compared with the control groups. The conclusion: the present study was conducted to, the treatment with Nandrolone decanoate doping for the periods (one, two and three months) caused observable deterioration in the functional performance of both hepatic and renal tissues.

Keywords: *Nandrolone decanoate doping, Hepatic and renal tissues functional performance, Patho-histological effects, Physiological and biochemical properties of the blood.*

Introduction

Anabolic androgenic steroids (AAS) are considered of the most important compounds used in medicine, which are illegal for bodybuilders and the players who use these steroids in order to increase the mass of the their muscles and improve their functions. [1, 2]. They are synthetic derivatives from the male sex hormone (Testosterone). They are tiny particles that can be distributed into various bodies' tissues [3], anabolic androgenic steroids have two main effects on the human body, the first is anabolic or that the effect of muscle building includes an increase in the protein formation, which leads to muscle growth and increase in size. The second effect, however, is androgenic or

stimulating masculinity, which comprises the production of sperms, coarse voice, growth of hears. Although the pharmaceutical industry of anabolic androgenic steroids already has low anabolic and androgenic influences, normally referred to as (Anabolic steroids),but both of the anabolic and the androgenic impacts are inseparable [4].

Anabolic steroid hormones disrupts or disables the endocrine glands since it is already considered biologically active compounds in the mammals [5,6].

In males, the hormonal neurotransmitter signals transferred the information towards the hypothalamic – pituitary axis and the interstitial tissue of Leydig and Sertoli cells, the germinal epithelium tissue lining of the seminiferous tubules, and as a result, fertility can be inhibited through changing the functional performance of tissues and cells, which are previously mentioned. This, in turn, plays an essential role in assessing the risks related to the use of steroids in order to improve the livestock used for human consumption through the long term effect [7, 8, 9].

The Nandrolone decanoate (19-Nor-Testesterone) is considered of the anabolic androgenic steroids (AAS) that is widely used, and which is locally called Deca-Durabolin ester, the least used is Phenylpropioate ester. The Nandrolone decanoate has numerous negative effects on athletes and non-athletes alike. It is prescribed as a well as improving the physiological activities [10].

The masculinity influence of the Nandrolone decanoate stimulates the emergence of muscular characteristics by being linked to the androgen anesthetic compound, which is capable of increasing the mass and strength of the muscles, as receptors [11].

Furthermore, Nandrolone decanoate doping is used by athletes and in the medicine [12].

It works on increasing the body weight and muscle mass. It is also used to treat the chronic kidney diseases such as dialysis patients [13, 14], In addition to numerous other diseases such as old women osteoporosis [15] and the virus HIV that damages the muscle tissues [16].

However, the small doses of Nandrolone decanoate works on changing the levels of blood hemoglobin, while producing an enlargement or hypertrophy in the skeletal muscles [17]. The use of AAS was noticed to cause hepatotoxicity related to the fatty liver disease [18].

Study Objectives

- Diagnosing the effects of Nandrolone decanoate on the hepatic and renal tissues for albino male rats through the histological examination.

- Studying the influences of this steroid on the functional performance of the liver and kidneys through the assessment of some hepatic enzymes efficiency and the levels of the total bilirubin, urea, and creatinine in the serum.

- Evaluating the impacts of this type of doping on some of biochemical parameters of the blood such as the levels of triglycerides, total cholesterol, total protein, and albumin especially that it is widely used these days.

- Determining the side effects of the Nandrolone decanoate on the body weight and the relative weights of other body organs such as liver and kidneys.

Materials and Methods

Preparation of Laboratory Animals

Thirty albino male rats were used in the present study belong to the strain of Sprague-Dawley, their weights ranging between (180-250) g and their ages were less than twenty weeks. The study was carried out in the animal house of Biology department Faculty of Education for Girls, the floor of each animal cage was covered with sawdust, that was displaced twice or three times a week.

With regard to the feeding of rats was a water and protein enriched feed until the males became sexually matured (three months).

Preparation of Used Dose of Nandrolone Decanoate

Nandrolone decanoate doping (ND) with the dose of 250 mg/ml was purchased from Baghdad Pharmacy /Al-Najaf Al-Ashraf.

The stock solution was prepared according to the fallowing equation:-

N1 X V1 = N2 X V2

Concerning the dose of ND that used in the current study was 1mg/kg as mentioned by [19].

The Experimental Groups

First group: was considered a control group, contained (15) male rats were divided into three equal subgroups

- A group was injected with normal saline solution (0.9%) one time at week for only one month.
- A group was also administered with normal saline once a week for two months.
- The last group was subjected to (0.9%) of normal saline solution one time at week for three months.

Whereas, the second group was included (15) rats, divided into three equal subgroups

- A group was received (1mg/kg) the Nandrolone decanoate doping (ND) once a week for one month.
- A group was injected with (ND) doping at the concentration of (1mg/kg) one time weekly for two months.
- Finally, a group was administered with (1mg/kg) of (ND) doping also one time at week for the period of three months.

All the treatments were intramuscular injection (in the muscle of the hind limb of rat).

Sacrificing of Animals and Collection of the Blood Samples

At the end of all treatments, the body weight for each rat was measured, the blood was collected by heart puncture to take (5ml) of blood was transferred to a gel tube, then the rat was anatomized to extract the liver, right and left kidneys, after the removing of the adipose tissues, the weights of these organs were recorded by the sensitive balance and then kept in plastic containers that contained 10% formalin to prepare the histological sections.

Preparation of the Serum Samples

The gel tubes that contained the blood centrifuged for (10) minutes at (3000) rpm to separate the serum, then the serum transferred into the serum tubes were kept in -4C for the study of blood biochemical criteria.

The Biochemical Study

Estimation of Aspartate Amino-transferase (AST) Activity in the Serum

Regarding the effectiveness of AST enzyme in the serum, was estimated by using the kits of Biolabo-France Company [20].

Estimation of Alanine Amino-transferase (ALT) Activity in the Serum

According to [21] the ALT effectiveness was determined, the kits were equipped by Biolabo- France company and the absorbance was read by the using of spectrophotometer at (340) nm.

Estimation of Alkaline Phosphatase (ALP) Activity in the Serum

To measure the effectiveness of ALP enzyme, the method that described by [21] was used and the kits equipped by Biolabo- France company. The activity of ALP was evaluated at (510) nm.

Estimation of Total Bilirubin Level in the Serum

With regard to total bilirubin level, the method of [22] and the kits of France company (Biolabo) were used at the absorbance of (546) nm.

Estimation of Total Protein Level in the Serum

The level of total protein was determined according to [23], by using the Biuret reagent, which purchased from Biolabo-France company. The spectrophotometer was used to read the absorbance at (550) nm.

Estimation of Albumin Level in the Serum

Concerning the serum albumin level, was detected by using Bromocresol green from Biolabo-France company at PH (4.2) and the absorbance was (650) nm [24].

Estimation of Total Cholesterol in the Serum

This parameter was evaluated according to the method that described by (21), Biolabo-France company equipped the kits, and the absorbance was read at (500) nm.

Estimation of Triglycerides Level in the Serum

The kits were purchased from Biolabo-France company and the absorbance recorded by using the spectrophotometer at (500) nm [21].

Estimation of Creatinine level in the Serum

To estimate this index, the kits were equipped by Biolabo-France Company. Jaffe reaction was occurred according to the method of [25].the absorbance was (490) nm by using the spectrophotometer.

Estimation of urea level in the serum

In relation to serum urea level, the kits purchased from Biomerieux-France company , and according to the method of [21] the absorbance was recorded by the spectrophotometer at (550)nm.

The Histological Study

Preparation of the histological sections for liver, right and left kidneys was according to the methods described by [26].

Lastly, the statistical analysis of the present study was depended upon the method of [27] by

The Statistical Analysis

using the Statistical Package Social Sciences (SPSS) , version [21], and Analysis of Variance (ANOVA) , then the Least Significant Difference at (P<0.05) level.

Results

Effect of Nandrolone Decanoate on the Body Weight

According to the results of present study , the weight gain of the group that treated with the doping for one month was 13.30 ± 2.24 , and the group injected with Nandrolone deaconate(ND)for two months was 56.40 ± 6.52 , while the group that received(ND) for three months was 71.40 ± 8.33 compared to the control groups as shown in Table (1)

Table 1: Effect of injection periods with Nandrolone decanoate doping (ND) on the body weight

Treatments	Sample numbers	Weight gain/g
1-The first control group	5	6 ± 0.31 a
2-The second control group	5	8.80 ± 0.77 a
3-The third control group	5	12.60± 1.28 a
4-The group that treated with Nandrolone decanoate for one month	5	13.30± 2.24 ab
5- The group that treated with Nandrolone decanoate for two months	5	56.40 ± 6.52 c
6- The group that treated with Nandrolone decanoate for three months	5	71.40 ± 8.33 d
LSD=14.545		

The same letters represent, no significant differences between means at (P<0.05) level.
The different letters indicate to the significant differences between means at (P<0.05) level.

Concerning the relative weights of liver , right kidney ,and left kidney, AST,ALT,ALP effectiveness ,levels of total bilirubin ,total protein, albumin ,total cholesterol, triglycerides, creatinine and urea were showed a significant increase (P<0.05) when the groups that administered with Nandrolone decanoate for (one , two and three) months compared with the control groups , Tables (2,3,4,5,6,7,8,9,10,11,12,13 and 14) respectively. Furthermore, notable differences (P<0.05) were observed in those parameters when the periods of treatment with the Nandrolone decanoate doping have compared with each other.

Table 2: Effect of injection periods with Nandrolone decanoate doping (ND) on the relative weight of liver

Treatments	Sample numbers	Liver weight/mg-100g of body weight
1-The first control group	5	8.06 ± 0.27 a
2-The second control group	5	8.30 ± 0.14 a
3-The third control group	5	8.95 ± 0.18 a
4-The group that treated with Nandrolone decanoate for one month	5	10.18 ± 0.5 b
5- The group that treated with Nandrolone decanoate for two months	5	14.86 ± 0.16 c
6- The group that treated with Nandrolone decanoate for three months	5	19.30 ± 0.29 d
LSD=0.950		

Table 3: Effect of injection periods with Nandrolone decanoate doping (ND) on the relative weight of right kidney

Treatments	Sample numbers	Right kidney weight /mg-100g of body weight
1-The first control group	5	0.71 ± 0.05 a
2-The second control group	5	0.73 ± 0.03 a
3-The third control group	5	0.74 ± 0.01 a
4-The group that treated with Nandrolone decanoate for one month	5	0.98 ± 0.13 b
5- The group that treated with Nandrolone ddecanoate for two months	5	1.55 ± 0.11 c
6- The group that treated with Nandrolone decanoate for three months	5	2.03 ± 0.08 d
LSD= 0.216		

Table 4: Effect of injection periods with Nandrolone decanoate doping (ND) on the relative weight of left kidney

Treatments	Sample numbers	Left kidney weight/mg-100g of bodyweight
1-The first control group	5	0.78 ± 0.06 a
2-The second control group	5	0.79 ± 0.04 a
3-The third control group	5	0.85 ± 0.23 a
4-The group that treated with Nandrolone decanoate for one month	5	1.10 ± 0.14 b
5- The group that treated with Nandrolone decanoate for two months	5	1.60 ± 0.15 c
6- The group that treated with Nandrolone decanoate for three months	5	2.13 ± 0.10 d
LSD= 0.235		

Table 5: Effect of injection periods with Nandrolone decanoate doping (ND) on the AST activity

Treatments	Sample numbers	AST activity (unit/L)
1-The first control group	5	33.40 ± 1.32 a
2-The second control group	5	32.40 ± 1.53 a
3-The third control group	5	32.92 ± 1.47 a
4-The group that treated with Nandrolone decanoate for one month	5	65.20 ± 1.93 b
5- The group that treated with Nandrolone decanoate for two months	5	110.60 ± 3.57 c
6- The group that treated with Nandrolone decanoate for three months	5	146.80 ± 3.15 d
LSD=7.618		

Table 6: Effect of injection periods with Nandrolone decanoate doping (ND) on the ALT activity

Treatments	Sample numbers	ALT activity (unit/L)
1-The first control group	5	43.48 ± 1.26 a
2-The second control group	5	41.60 ± 1.05 a
3-The third control group	5	42.46 ± 1.89 a
4-The group that treated with Nandrolone decanoate for one month	5	79.40 ± 0.97 b
5- The group that treated with Nandrolone decanoate for two months	5	123.60 ± 2.92 c
6- The group that treated with Nandrolone decanoate for three months	5	162.60 ± 3.32 d
LSD=6.905		

Table 7: Effect of injection periods with Nandrolone decanoate doping (ND) on the ALP activity

Treatments	Sample numbers	ALP activity (unit/L)
1-The first control group	5	146.28 ± 8.15 a
2-The second control group	5	144.20 ± 5.98 a
3-The third control group	5	148.20 ± 7.14 a
4-The group that treated with Nandrolone decanoate for one month	5	235.48 ± 10.11 b
5- The group that treated with Nandrolone decanoate for two months	5	343.20 ± 9.21 c
6- The group that treated with Nandrolone decanoate for three months	5	440.20 ± 13.04 d
LSD=86.76		

Table 8: Effect of injection periods with Nandrolone decanoate doping (ND) on the total bilirubin level

Treatments	Sample numbers	Total bilirubin level mg/dL
1-The first control group	5	0.60 ± 0.04 a
2-The second control group	5	0.52 ± 0.07 a
3-The third control group	5	0.48 ± 0.05 a
4-The group that treated with Nandrolone decanoate for one month	5	0.94 ± 0.08 b
5- The group that treated with Nandrolone decanoate	5	1.36 ± 0.44 c

for two months		
6- The group that treated with Nandrolone decanoate for three months	5	1.81 ± 0.15 d
LSD=0.184		

Table 9: Effect of injection periods with Nandrolone decanoate doping (ND) on the total protein level

Treatments	Sample numbers	Total protein level mg/dL
1-The first control group	5	6.34 ± 0.16 a
2-The second control group	5	6.36± 0.12 a
3-The third control group	5	6.42 ± 0.26 a
4-The group that treated with Nandrolone decanoate for one month	5	7.04 ± 0.13 b
5- The group that treated with Nandrolone decanoate for two months	5	7.74 ± 0.33 c
6- The group that treated with Nandrolone decanoate for three months	5	8.62 ± 0.15 d
LSD=0.479		

Table 10: Effect of injection periods with Nandrolone decanoate doping (ND) on the albumin level

Treatments	Sample numbers	Albumin level mg/dL
1-The first control group	5	2.50 ± 0.11 a
2-The second control group	5	2.52 ± 0.15 a
3-The third control group	5	2.56 ± 0.06 a
4-The group that treated with Nandrolone decanoate for one month	5	3.04 ± 0.18 b
5- The group that treated with Nandrolone decanoate for two months	5	3.62 ± 0.24 c
6- The group that treated with Nandrolone decanoate for three months	5	4.46 ± 0.12 d
LSD=0.442		

Table 11: Effect of injection periods with Nandrolone decanoate doping (ND) on the total cholesterol level

Treatments	Sample numbers	Total cholesterol level mg/dL
1-The first control group	5	88.80 ± 1.24 a
2-The second control group	5	93.03 ± 1.84 b
3-The third control group	5	103.40 ± 1.40 b
4-The group that treated with Nandrolone decanoate for one month	5	137.60 ± 3.28 c
5- the group that treated with Nandrolone decanoate for two months	5	170.40 ± 9.19 d
6- The group that treated with Nandrolone decanoate for three months	5	245.80 ± 7.37 e
LSD=16.653		

Table 12: Effect of injection periods with Nandrolone decanoate doping (ND) on the triglycerides level

Treatments	Sample numbers	Triglycerides level mg/dL
1-The first control group	5	60.76 ± 6.51 a
2-The second control group	5	68.89 ± 5.2 a
3-The third control group	5	73.11 ± 0.01 a
4-The group that treated with Nandrolone decanoate for one month	5	106.40 ± 2.50 c
5- The group that treated with Nandrolone decanoate for two months	5	138.20 ± 3.96 d
6- The group that treated with Nandrolone decanoate for three months	5	159.40 ± 4.04 e
LSD=13.828		

Table 13: Effect of injection periods with Nandrolone decanoate doping (ND) on the creatinine level

Treatments	Sample numbers	Creatinine level mg/dL
1-The first control group	5	0.28± 0.03 a
2-The second control group	5	0.19± 0.005 a
3-The third control group	5	0.25± 0.013 a
4-The group that treated with Nandrolone decanoate for one month	5	0.58± 0.03 b
5- The group that treated with Nandrolone decanoate for two months	5	1.02± 0.086 c
6- The group that treated with Nandrolone decanoate for three months	5	1.53± 0.089 d
LSD=0.178		

Table 14: Effect of injection periods with Nandrolone decanoate doping (ND) on the urea level

Treatments	Sample numbers	Urea level mg/dL
1-The first control group	5	16.40± 1.15 a
2-The second control group	5	` 14.54± 4.73 a

3-The third control group	5	20.30± 3.66 a
4-The group that treated with Nandrolone decanoate for one month	5	32.80± 2.17 b
5- The group that treated with Nandrolone decanoate for two months	5	48.33 ± 0.70 c
6- the group that treated with Nandrolone decanoate for three months	5	63.98± 4.61 d
LSD=10.634		

Histological Examination of Liver and Kidney Sections at Rat Males

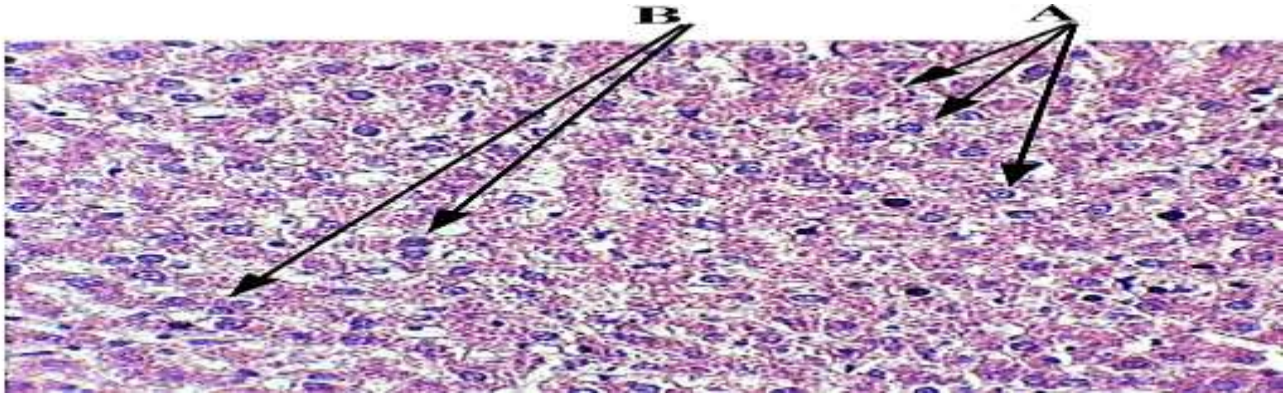


Figure 1: Section in the liver at control group: normal hepatocytes (A) binucleated hepatocytes (B) .Staining hematoxylin-eosin (400X)

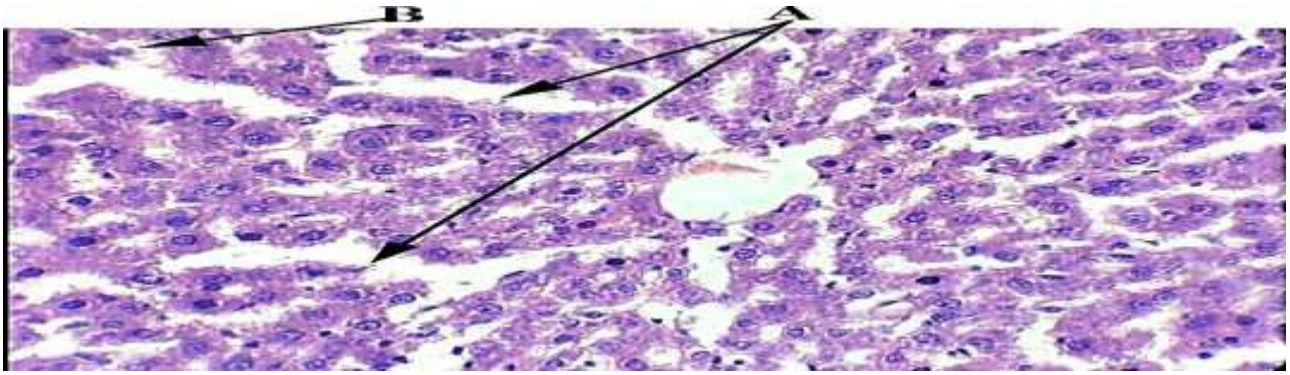


Figure 2: Section in the liver at group that injected with Nandrolone decanoate(ND) for one month: dilatation of hepatic sinusoids(A) necrosis of some hepatocytes(B). Staining hematoxylin-eosin (400X)

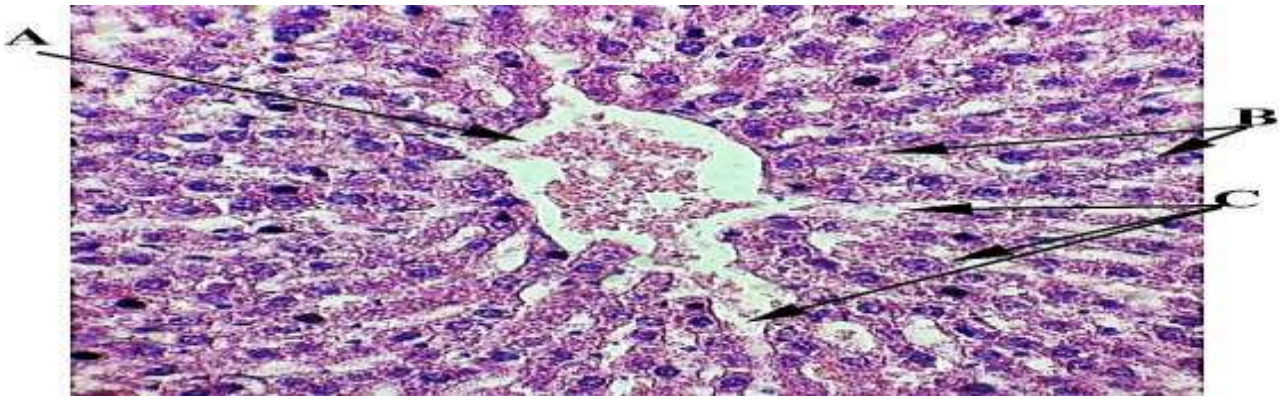


Figure 3: section in the liver at group that injected with (ND) for two months: dilatation of liver lobule central vein (A) necrosis of some hepatocytes(B) disarrangement of hepatic strands(C). Staining hematoxylin-eosin (400X)

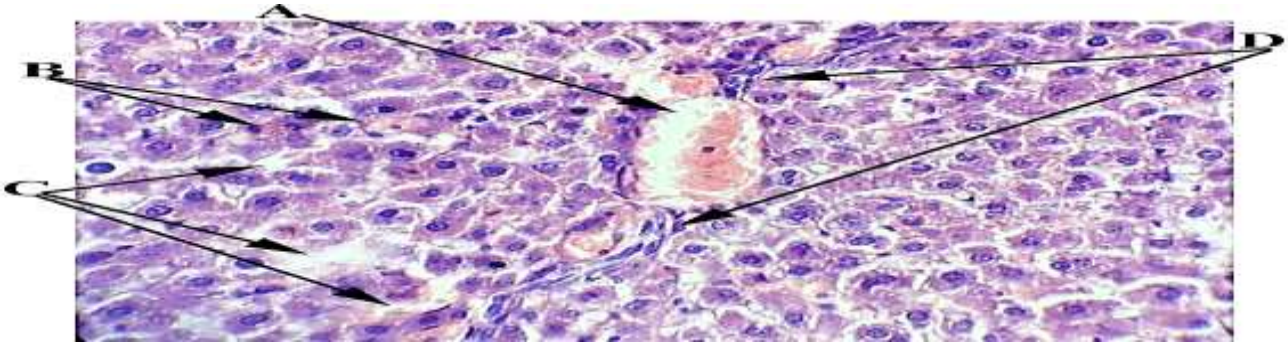


Figure 4: Section in the liver at group that injected with(ND)for three months: dilatation of liver lobule central vein with hemorrhage(A)hemorrhage within the hepatocyte(B)cytoplasmic vacuolation of hepatocytes due to fatty

degeneration(C)severe infiltration of inflammatory cells around the central vein(D). Staining hematoxylin-eosin (400X)

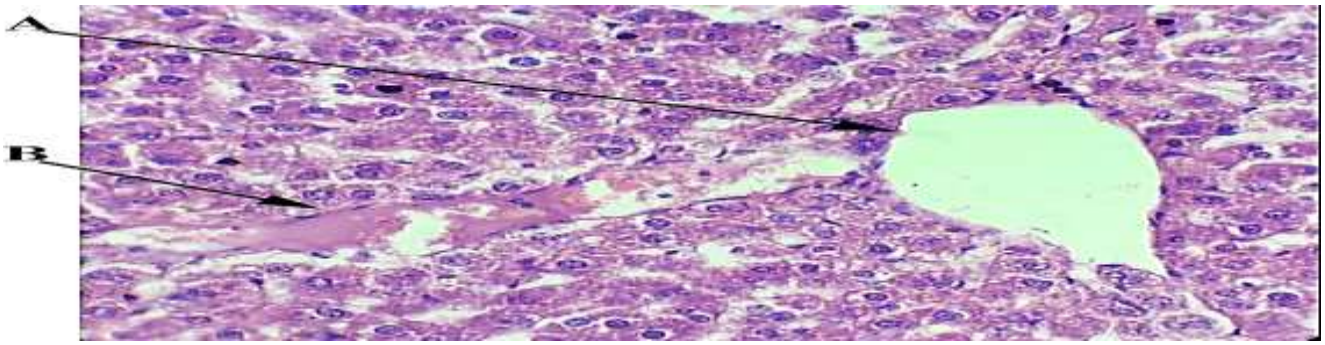
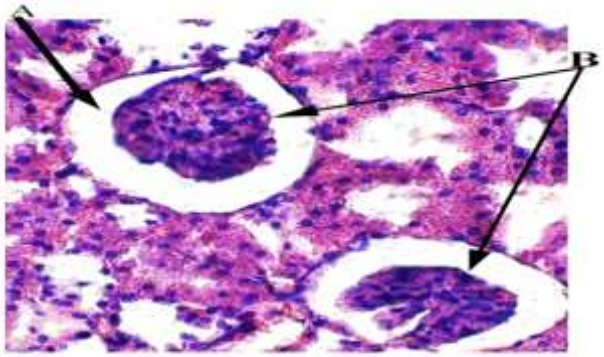
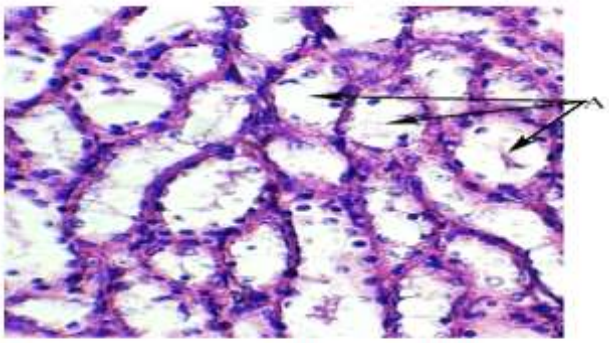


Figure 5: section in the liver at group that injected with (ND) for three months: severe destruction of liver lobule central vein (A) hemorrhage within the interstitial tissue of hepatocytes(B) Staining hematoxylin-eosin (400X)



Figure(6)section in kidney cortex at control group:normal capsule of renal glomerulus(A) normal glomeruli (B). Staining hematoxylin -eosin (400X).



Figure(7)section in kidney medulla at control group: normal renal tubules(A) Staining hematoxylin-eosin(400X)

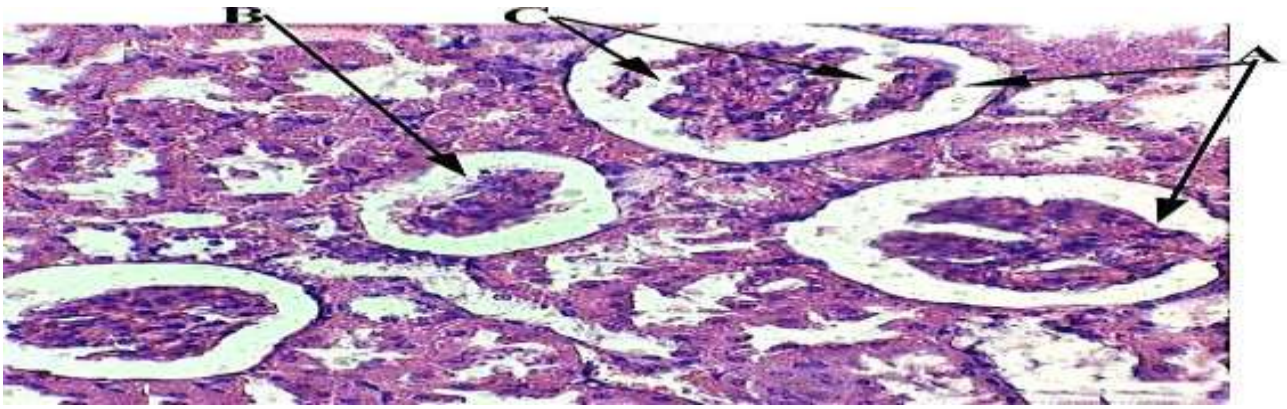


Figure 8: Section in the kidney cortex at group that injected with(ND)for one month: hypertrophy of renal glomeruli(A)degeneration of renal glomerulus squamous epithelial cells(B)necrosis of renal glomerulus squamous epithelial cells(C).Staining hematoxylin-eosin(400X)

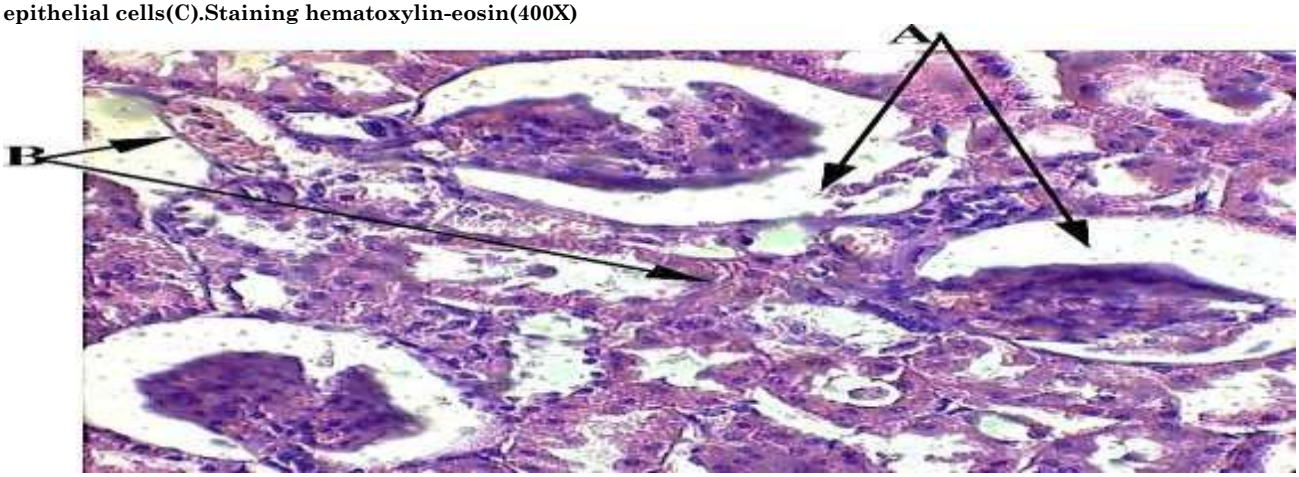


Figure 9: Section in the kidney cortex at group that injected with (ND)for two months: increase of Bowman's space (A)hemorrhage within the interstitial tissue of cortex(B). Staining hematoxylin-eosin (400X)

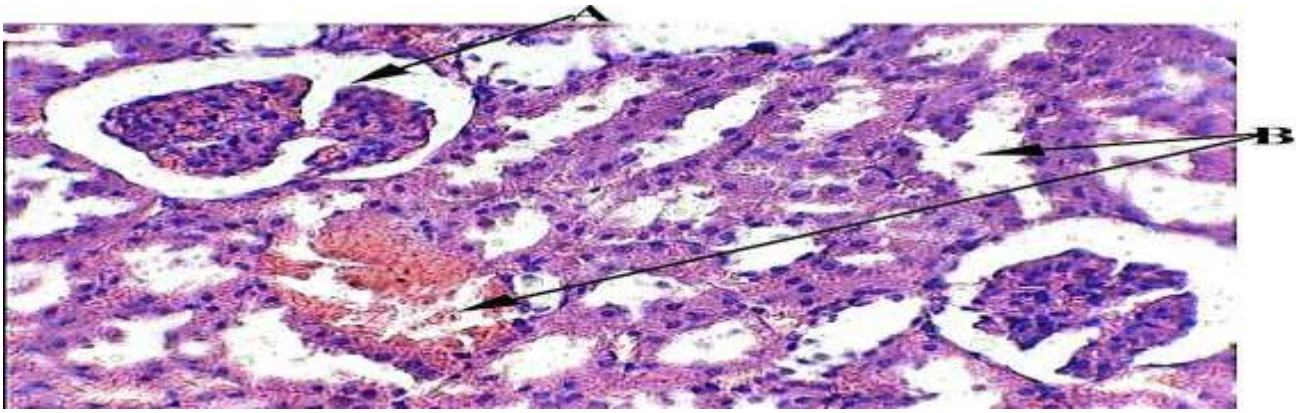


Figure 10: Section in the kidney cortex at group that injected with (ND) for three months: hypertrophy of renal glomerulus (A) edema and severe hemorrhage within the interstitial tissue of cortex (B). Staining hematoxylin-eosin (400X)

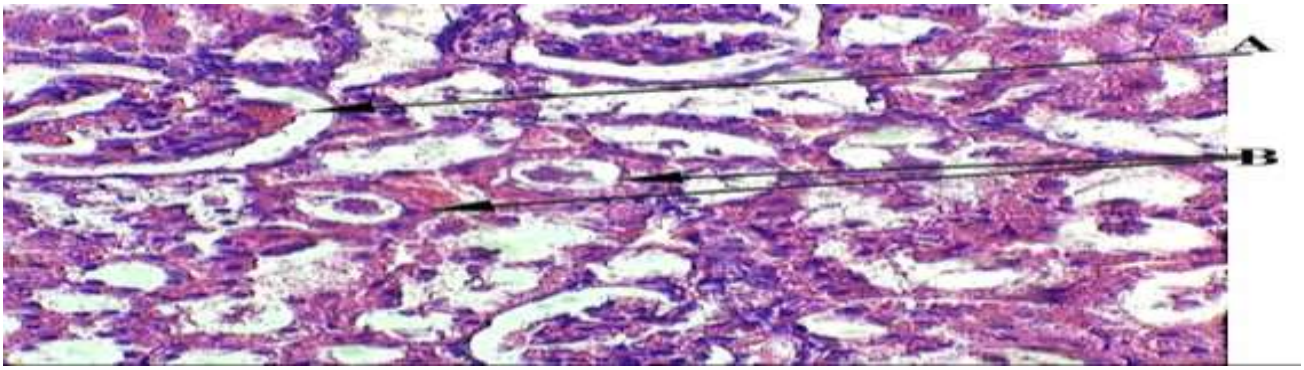


Figure 11: Section in the kidney cortex at group that injected with (ND) for three months: hemorrhage in the renal glomerulus(A)hemorrhage in the proximal convoluted tubules (B).Staining hematoxylin-eosin(400X)

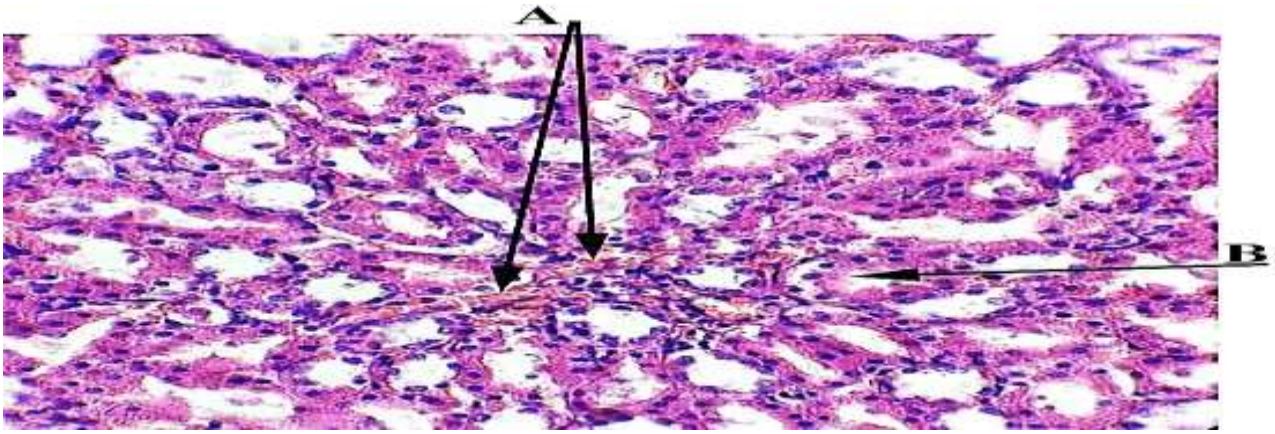


Figure 12: Section in the kidney medulla at group that injected with(ND)for one month: severe hemorrhage within the interstitial tissue of kidney medulla(A)dissociation of simple cuboidal cells lining of renal tubules from the basement membrane(B).Staining hematoxylin-eosin(400X)

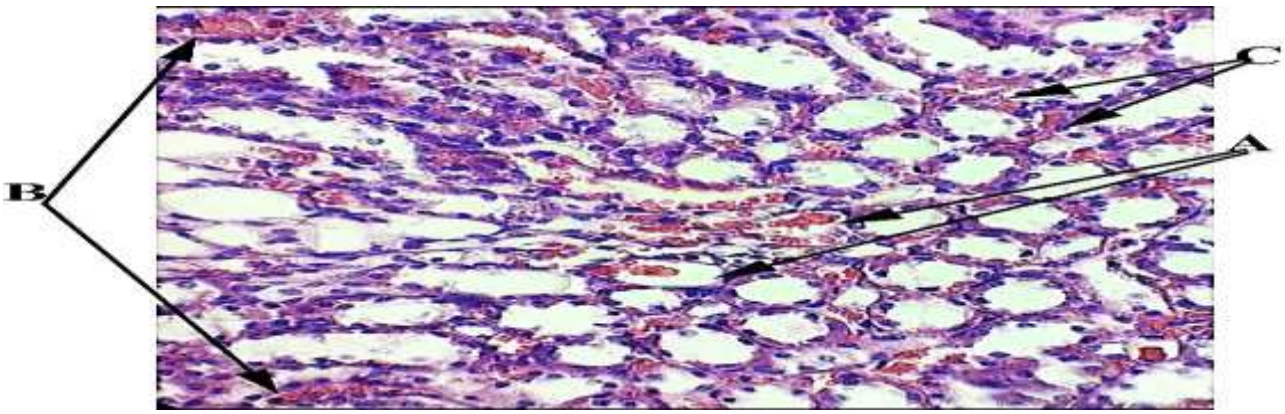


Figure 13: Section in the kidney medulla at group that injected with(ND)for two months: dissociation of simple cuboidal cells lining of renal tubules from the basement membrane, and aggregation of red blood corpuscles within the renal tubules(A) severe hemorrhage in the renal tubules(B) ,and within the interstitial tissue of medulla(C).Staining hematoxylin-eosin (400X)

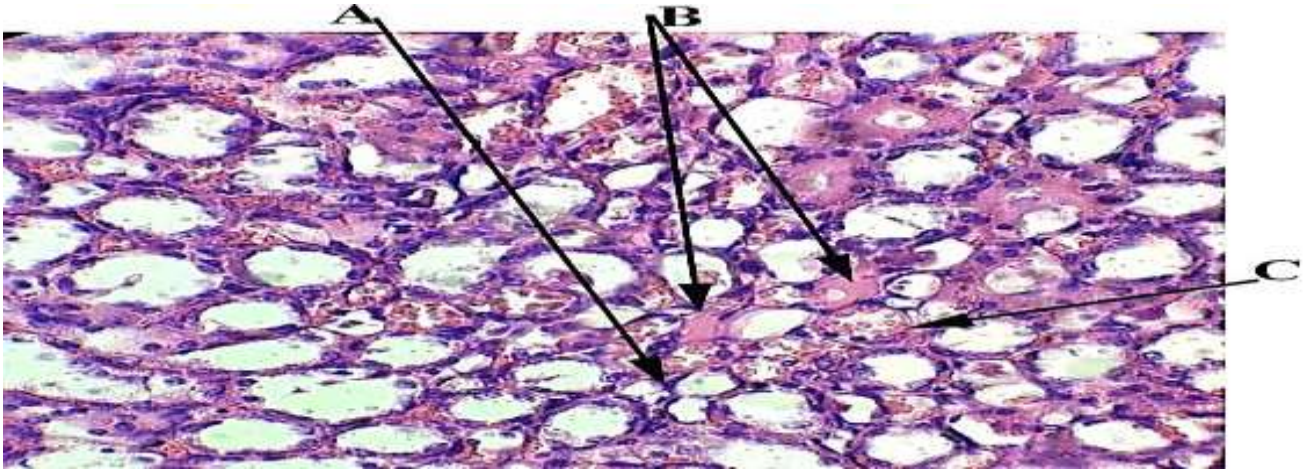


Figure14: Section in the kidney medulla at group that injected with(ND)for three months: stricture of some renal tubules diameters(A) severe hemorrhage within the interstitial tissue of medulla(B)appearance of red blood corpuscles in the renal tubules(C).Staining hematoxylin-eosin (400X)

Discussion

Effect of Nandrolone Decanoate on the Body Weight

The results of the current study indicated that there is a significant increase in the

body weight for the groups that treated with Nandrolone Decanoate when compared with the non-treated, control groups. The results, however, concurred with many previous ones. [1,28,29]. The increase in the body weight may have happened due to the rise in the consumption of food and water by the animals that treated with Nandrolone Decanoate, and the effect of the testosterone which may be worked as a stimulator for the protein bio-manufacturing and improved the muscles by increasing the bio-mass of the different body tissues, which, in turn, causes an apparent increase in the body weight, as was confirmed by[30].

Some studies explained the increase in body weight of both males and females, compared to the control group, to the obvious increment in the rate of food and water consumption of the test groups that injected with Nandrolone Decanoate. However, this increase in food and water consumption may be due to the fact that the Nandrolone decanoate has altered the metabolism in the skeletal muscles. [31,32,33]. Other studies noted that the groups treated with AAS have altered the protein formation process in general, as well as the type of fibers that forms the muscular cells; therefore, it has resulted in an increase in the body weight of the albino rats [34]. In addition, [35] have mentioned, treating HIV patients with Nandrolone decanoate may increase the mass of the depleted body. In another study, it was noticed that treating albino rats with Nandrolone decanoate for eight weeks have resulted in a raise in the body weight of the rats as well as a change in the glucose and fat metabolism in general [19]. This increment may be referred to the fact that injecting the males with Nandrolone decanoate have affected the hunger and satiety centers that are located in the hypothalamus area, which have resulted in a rise in the total consumption rate of food and water for the treated rats, and ultimately, an increase in body weight.

It is possible that this rise in the body weight is due to the change in the thyroid activity rate caused by the Nandrolone decanoate, which in turn have caused an increment in the rate of food and water consumption resulting in an increase in the body weight. [36] have postulated that the weight of the thyroid increased when treating the albino rats with Nandrolone decanoate for eight consecutive months and a decrease in the levels of TSH .[37] have mentioned that treating the rats with Nandrolone decanoate for eight months have affected the blood pressure, the fat features as well as the hepatic functions for bodybuilders, in addition, there was an increase in body mass, systolic blood pressure, a decrease in the levels of high density lipoproteins and cholesterol, with no changes to the hepatic amine group transporting enzymes.

Many studies [38, 14, 39] have proved that using Nandrolone decanoate as a treatment or therapy helps reviving body weight for the HIV patients as well as dialysis patients. The

increment in the body weight may be due to the observable increase in the levels of total cholesterol and triglycerides which were both recorded in the current study, as well as many studies have confirmed that the increase in the body mass and weight for the treated groups is referred to the significant rise in the levels of free fats [38,40].The increase in body weight of the treated groups perhaps due to a significant raise in the main metabolism rate, which also resulted in an increment in the bio-manufacturing processes of proteins, enzymes, and metabolic activities of all body cells. Some references have indicated that injecting testosterone results in a 15% increase of main metabolism process [30].

It is also probable that some of this body weight increment is due to the notable increase in the relative weight of some organs like liver and kidneys (Both left and right) which were documented in the present study. Finally, the increase of body weight of the injected rats with Nandrolone decanoate may have occurred because these types of steroid affect the activity of the adrenal gland. Contrast to all that preceded both of [41] and [42] have noticed that body weight decreased when the injecting process was accompanied with extra exercises.

Effect of Nandrolone Decanoate on the Relative Weight of Liver

The results of the current study showed a significant increase in the relative weight of the liver for the groups that treated with Nandrolone Decanoate compared to the control groups. This result was incompatible with other studies [1, 43] that found the group treated with Nandrolone decanoate did not have any changes in the weights of spleen, liver, adrenal gland, seminal vesicles as well as testes , but rather having a negative effect on liver functions.

This may be referred to the patho-histological changes in liver that were recorded throughout the study. Some studies have pointed that injecting smaller doses of Nandrolone decanoate caused congestion in the hepatic tissue as well as a remarkable increment in the weight of the organ. However, higher doses of the Nandrolone decanoate caused a decrease in the liver weight, fibrosis, increment in collagen content of the parenchyma tissue at the treated rats [29, 44]. In another study, the increase in liver weight of the male rats that treated with Nandrolone decanoate fluctuated between 19 to 36% by means of bio-stimulation of the mentioned steroid [45]. It is possible that this rise in liver weight may have attributed to the significant increase in the levels of total cholesterol, triglycerides, total protein, albumin, and effectiveness of the hepatic enzymes that were documented in this study. That however may have led to a significant increment in liver activity which also led, in turn to a rise in liver mass and ultimately a notable increase in liver weight, since it is the organ responsible for regulation of the total cholesterol and triglycerides levels in the body, as well as its activity in the manufacturing of all kinds of protein particles [30].

Finally, this increment in the liver weight may be due to the significant increase in urea and creatinine levels that were documented in this study, because the main function of the hepatic tissues is to rid the body from the toxic materials among which are the metabolic products that are pointed out through converting them to less toxic secondary compounds and extruded it out of the body. Therefore, the observable raise in these standards may have caused organ enlargement and subsequent increase in the liver weight.

Effect of Nandrolone Decanoate on the Relative Weight of Kidneys

The results of the current study have indicated an increment in the weight of the kidneys for the groups treated with Nandrolone decanoate when compared with the control groups, this study have agreed with other similar studies of [29] and [46] who found that the weight of both kidneys as well as their diameter have significantly increased as a result of being treated with Nandrolone decanoate for eight weeks. According to them, this increase was due to the congestion of the renal tissues. Other studies have noted that the kidney weight has increased by 30% when animals were treated with Nandrolone decanoate for eight weeks. [47,48].

It is possible that the raise in the kidney weight has happened because of the patho-histological alterations that are diagnosed in the renal tissues among which are the hypertrophy of the renal glomeruli , the

appearance of edema with a dense accumulation of red blood corpuscles within the interstitial tissue of the cortex and increase of Bowman's space, in addition to bleeding in the convoluted tubules, as well as the detachment of simple cuboidal cells lining of renal tubules from the basement membranes, and other negative effects due to use of this type of doping .

Effect of Nandrolone Decanoate on the AST, ALT and ALP Enzymes Activity in Serum

The results of the current study indicated a significant increase in the effectiveness of hepatic enzymes such as ALP, ALT, and AST for the groups that treated with Nandrolone decanoate as compared with the control groups, which in turn, agrees with other studies [1,44].

The increment in the effectiveness of these enzymes may be due to the pathological influences of Nandrolone decanoate on the hepatic tissues for the males injected with this type of stimulant which caused an increase in liver size and its color was changed. It is possible that, these enzymes were liberated from the cytoplasm of the cells to the blood stream because of the hepatic cells necrosis, enlargement, and the torn of plasma membranes that surrounding them. The present study recorded numerous variations in the hepatic tissues, among which are necrosis, bleeding, dilatation in the hepatic sinusoids of the liver, cytoplasmic vacuolation of hepatocytes due to the fatty degeneration, severe invasion of inflammatory cells were accumulated around the central vein, serious damage to the central vein of liver lobule, in addition to some bleeding veins.

Another study have illustrated that the assessment of transferable enzymes effectiveness of amino group is considered the most sensitive to determine the toxic effects of the hepatic tissues [49,1] added that the increase in the levels of those enzymes (AST, ALT and ALP) as a result of injecting Nandrolone decanoate lead to hepatic toxicity. Later study indicated that the treatment with anabolic androgenic steroids (AAS) for long time raises the effectiveness of these hepatic enzymes and increasing the chances of getting deadly liver bags (abscess), in addition to other histological and pathological hepatic alterations, as well as liver cancer [50,51] Have proposed that the continuation to use AAS for longer periods stimulates the significant increase in the activity of hydrolysis enzymes, which exist in the hepatic tissue lysosomes. Another study added that Nandrolone decanoate is considered the most powerful stimulant in altering the effectiveness of some enzymes, among which is glutathione transferase enzyme in the hepatic tissues, the group that treated with the normal dose of Nandrolone decanoate revealed an increase in the activity of two hepatic enzymes, which were ALT and AST in the male rates [1,52].

In addition to what have preceded,[33]confirmed that the effectiveness of AST has significantly increased in both male and female rats were treated with Nandrolone decanoate as compared with the control groups. However, the effectiveness of ALT enzyme had no changes at all when comparing the treated group with the control groups. It is also worth mentioning that ALP is considered one of the most sensitive hepatic enzymes for any type of hepatic injury or damage, it is released in large amounts to the blood stream when the hepatic tissue suffers any oxidative stress [53]. Therefore, the registered increment in the effectiveness of this enzyme throughout the current study indicates that the Nandrolone decanoate doping has severely affected the hepatic tissues to the extent that it was liberated to the blood directly from the cells.

5-Effect of Nandrolone decanoate on the total bilirubin, total protein and albumin levels

The levels of total bilirubin, total protein, and albumin for the groups that treated with Nandrolone decanoate were showed a significant increment compared to those of the control groups, these data are different from a study by (54), who indicated that treating rats with Nandrolone decanoate for six weeks did not appear any noticeable change in the level of albumin at serum. It was also in agreement with [1], which revealed that treating rats with Nandrolone decanoate for five weeks have actually caused notable decrease in the total protein and total bilirubin levels.

On the other hand, it agreed with other study, which confirmed that treating rats with Nandrolone decanoate for eight weeks

resulted in a remarkable increase in the bilirubin levels at the serum [29]. The results may have explained to the patho-histological effects of the Nandrolone decanoate on the hepatic tissues, that resulted in damaging the plasma membranes of the hepatocytes via lipid peroxidation, which also increased the production rate of reactive oxygen species, especially hydroxyl radical, hydrogen peroxide, the radical anion of superoxide , and other kinds of the toxic free radicals , all of which may have contributed to the damage inflected on the high-sensitivity particles such as carbohydrates, proteins, fats, and the DNA bases.

The toxicity may have also included the other cellular components of the hepatic tissues, which have increased the bilirubin levels in blood. The increment in the levels of those indicators, may also be due to the internal or external blockages in the bile ducts of the liver because of the pathological influences of the steroid was used in the current study, that negatively affected the significant increase in bilirubin levels. Many studies have confirmed that bilirubin level in the serum is considered an important marker to the diagnoses and detection of obstructive jaundice in the liver [55,56]. In addition to what preceded, the increase in the bilirubin levels may be referred to the deteriorative effects of the Nandrolone decanoate on the membranes of red blood corpuscles for it may have caused necrosis in the membranes of these cells which have also resulted in a rise in the levels of bilirubin in the blood stream. Concerning the significant increment in the total protein levels at the serum for the groups treated with Nandrolone decanoate, it may be caused by the positive stimulation of this kind of steroid to increase the biological synthesis of protein particles and rise their levels in the serum subsequently.

This, however, resulted in a notable increase in the levels of total protein in the non-muscular tissues, which was also indicated by [30].This raise may also be a result of the noticeable increment in the albumin level at the serum for the male rats that treated with Nandrolone decanoate, which was documented in this study, and since the latter is the most abundant in the plasma [30], its significant increase in the serum may trigger or cause another remarkable rise in the total protein levels.

Lastly, the notable increase in the total protein and albumin levels at the serum, perhaps due to the histological and pathological alterations caused by Nandrolone decanoate which, in turn, causes partial or total necrosis of the tissue contents and subsequent egression all of these components to the blood stream, including proteins, and increasing their levels there as well.

Effect of Nandrolone Decanoate on the Total Cholesterol and Triglycerides Levels

With respect to the significant increment in the levels of total cholesterol and triglycerides at the male rats treated with Nandrolone decanoate compared to the control groups, was concordant with the study of [57], who confirmed that the treatment with testosterone or anabolic steroids are closely associated with the increased risk of high blood pressure, adverse changes in the lipid profiles, coronary heart diseases, heart failure, various blood thrombi and myocardial infarction, which can lead to sudden death . As such, the study also agreed with several other studies which noticed that the treatment with Nandrolone Decanoate significantly increases the levels of total cholesterol and triglycerides [1,28,54].

The rise in the levels of these standards is likely to be due to the anabolic impacts of the type of doping that used in the current study, which may have notably increased the rate of bio-processing of total cholesterol and triglycerides through its direct effects on the hepatic tissues, which are the primary precursor to the synthesis of these molecules, this would cause high serum levels. The raise in total cholesterol levels may be attributed mainly to increased levels of low-density lipoproteins under the detrimental influences of Nandrolone decanoate stimulant, as confirmed by some studies [54], which indicated that the treatment of male rats with Nandrolone decanoate significantly increases the levels of low-density lipoproteins and, conversely, decreases the levels of high-density lipoproteins by inducing or stimulating the vital effectiveness of the enzyme responsible for the catabolism of high-density lipoproteins molecules (HDL-catabolizing enzyme), it is the same for the hepatic enzyme that analyzes the triglycerides (Hepatic

triglyceride lipase HTGL). It is worth mentioning that the type of doping was used in the current study is one of the least effective stimulants to metabolize to estrogen than testosterone, so it has a high effectiveness in stimulating the hepatic enzyme that analyzes the triglycerides (HTGL) [54], which may lead to appearance of the bad physiological actions of testosterone on the features of high-density lipoproteins in contrast to low-density lipoproteins, resulting in a significant increase in levels of total cholesterol and triglycerides. Contrary, some studies have been noticed that people who are taking anabolic androgenic steroids (AAS) with workout have shown a remarkable reduction in the levels of low-density lipoproteins, total cholesterol, high-density lipoproteins and triglycerides [58]. A subsequent study also found that Nandrolone decanoate treatment for 14 weeks did not significantly change the total cholesterol and triglyceride levels in the blood (33)

Effect of Nandrolone Decanoate on the Creatinine and Urea Levels

The results of the present study showed a noticeable increase in the levels of creatinine and urea at the Nandrolone decanoate treated groups compared to the control groups. This finding agrees with many other studies [29,48].

The result of the current study may be explained to the negative effects of Nandrolone decanoate on the renal tissues, it is diagnosed by enlargement or hypertrophy of some renal glomeruli, increasing in the Bowman's space, hemorrhage in the renal glomeruli and interstitial tissue of cortex. Also, degeneration and necrosis of squamous epithelial cells of some renal glomeruli, which causes increased levels of creatinine and urea in the blood for a decrease in the removal rate of these high toxic particles (reduction in the rate of the glomerular filtration process).

Those standards are important indicators used in the clinical diagnosis to assess the degree of renal failure [30]. The increment of creatinine levels in serum of male rats that treated with Nandrolone decanoate is possibly due to an ulceration in the internal tissues of the kidney, shrinkage of mesangial cells of renal glomerulus, reduction of renal perfusion rate, or blockage in the lower urinary tract because the effect of various types of harmful free radicals that may have increased their production rate due to the negative influences of the doping. Or it may explain the rise in the level of creatinine to a decrease in the rate of kidney excretion as a result of the occurrence of blockages in the renal tubules due to the death of some simple cuboidal cells lining of renal tubules as well as egression of their cytoplasmic and nuclear contents which fall into the cavities of those tubules, causing the loss of ability to filter.

So, creatinine is a metabolically product that it is mainly excreted by the kidney through the glomerular filtration process and the loss of contact between the podocytes and the basement membranes of the renal glomeruli caused a defect or disorder in the blood filtration. In addition, the tubular necrosis also leads to notable increase in the creatinine levels [59], it is worth mentioning that tubular necrosis has been diagnosed in some sections of renal tissues which were belonging to male rats that injected with Nandrolone decanoate. As for the urea molecules, it is the final metabolic product of the protein break, so its level rises significantly when there is a decrease or reduction in the rate of glomerular filtration process and also when the renal tissues are injured or damaged, so the high levels of creatinine and urea in the blood are the most important clinical indices of renal failure [60].

Effect of Nanadrolone decanoate on the liver and kidneys tissues

The histological examination of male rats injected with Nandrolone decanoate revealed several histological changes when compared with the control groups.

These data are similar to a finding by [61], which indicated that the treatment with Nandrolone decanoate, whether it is for a long or short time caused many pathological alterations in the hepatic tissues, including an increase in the organ weight, size of hepatocytes, infiltration of multi-nucleated leukocytes, congestion in the interstitial tissue of binucleated hepatic cells, as well as congestion in the blood vessels and ducts due to an inflammatory response with intrahepatocytes fat deposition.

Other studies have stated that Nandrolone decanoate doping revealed numerous hepatotoxic effects comprising, increased collagen deposition in the parenchyma tissue

of the liver, expansion or dilatation of the central vein of the liver lobules and portal space (29,44,62).

In relation with the pathological variations of the right and left kidneys for Nandrolone decanoate treated male rats were consistent with the findings of many other studies (10,63), who pointed to the scleroglomerulus, emergence of edema in other renal glomeruli , as well as occurrence of the tubular degeneration and multiple foci of blood congestion within the renal tissues. Other studies have noted that the treatment of male rats with another type of testosterone, a testosterone undecanoate (TU) caused degeneration in the renal tissues by 25% (29, 64,65). With regard to the patho-histological influences on both liver and kidneys of animals that injected with Nandrolone decanoate are likely to account for the adverse effects of different detrimental free radicals, which may have increased their formation rate by this type of stimulant that caused various damages to the cellular components of the hepatic and renal tissues from the plasma membranes to the nuclear contents for these tissues.

Conclusion

- The injection of commonly used doping Nandrolone decanoate (ND) caused increase in the body weight, which may have resulted from the increment in levels of total cholesterol and triglycerides. Moreover, another possible reason is the increase in the relative weights of some organs such as liver and kidneys due to many of pathological changes in the cellular components of the tissues of those organs.
- The treatment with the doping for all study periods (one, two and three months) showed negative effects on the liver and kidney functions through the significant increase in the effectiveness of hepatic enzymes, total bilirubin, creatinine and urea levels.
- The microscopic examination of the liver and kidney sections, concluded that the continuation of the injection process of male rats with (ND) for all periods has caused adverse histological alterations in the tissues of the organs (liver, right and left kidneys) .

Recommendations

- Conducting further studies of other types of doping to diagnose the side effects associated with their use on the body weight and relative weights of some organs, as well as the physiological and biochemical criteria of the blood .
- Studying the detrimental effects of (ND)on the body weight and blood parameters at female rats to compare the results with the findings of the current study and determine which sex is more affected by this type of stimulant .
- Determining the pathological changes caused by the (ND) on the efficiency of the male reproductive system by studying its effects on the weights of sex accessory glands and some fertility parameters.
- Investigating the deteriorative impacts of over dose of (ND) on the body weight as well as the relative weights of some organs such as liver, kidney and various blood properties.
- Testing the patho-histological changes that can be caused by (ND) in other organs such as spleen, lungs and pancreas, in addition to the immunological effects by measuring the levels of certain serum interleukins.

References

1. Vieira RP, Franca RF, Damaceno-Rodrigues NR, Doihnikoff M, Caldini EG, Garvaiho CR, Ribeiro W (2008) Dose-dependent hepatic response to sub chronic administration of Nandrolone Decanoate , Med. Sci. Sports. Exerc. 40(5): 842-847.
2. Sjoqvist F, Garle M, Rane A (2008) Use of doping agents, particularly anabolic steroids, in sports and society. Lancet. 371(9627):1872-82.
3. Jassim AM, AL Zamely, HAN Abbas GH (2015) Study of testicular damage induced by dianabol and its effect on morphological and histological changes in albino male rats. (IOSR – JAVS). 8(8): 24-32.
4. Pope Jr, HG Wood, RI Rogol, A Nyberg, F Bowers, L Bhasin S (2013) Adverse health consequences of performance-enhancing drugs: An Endocrine Society scientific statement . Endocrine. Rev., 35: 341-375.

5. Shahidi NA (2001) A review of chemistry, biological action, clinical application anabolic-androgenic steroids. Clin ther. 23: 1355-1390.
6. Courant F, Pinel G, Bichon E, Monteau F, Antignac JP (2009) Development of a metabolomics approach based on liquid chromatography-high resolution mass spectrometry to screen for clenbuterol abuse in calves. Analyst, 134: 1637–1646.
7. Torres-Calleja J, Gonzalez-Unzaga M, DeCelis-Carrillo R, Calzada-Sanchex L, Pedron N (2001) Effect of androgenic anabolic steroids on sperm quality and serum hormone levels in adult male bodybuilders. Life. Sci., 68: 1769-1774.
8. Scarth JA, Kre K, van Ginkel L, Le Bizec, B De, Brabander H (2009) Presence and metabolism of endogenous androgenic-anabolic steroid hormones in meat-producing animals: a review. Food Addit. Contam. Part A .Chem. Anal. Control. Expo. Risk. Assess 26: 640-671.
9. Scarth JP, Clarke A, Teale P, Mill a, Macarthur R (2011) Detection of endogenous steroid abuse in cattle: results from population studies in the UK. Food .Addit. Contam. Part A .Chem. Anal. Control. Expo. Risk. Assess. 28: 44-61.
10. Ebeye OA, Ekundina VO, Osahon RI (2016) Histmorphological effect of nandrolone decanoate on the Hepatorenal tissues of adult Wister rat exposed physical activity .European. J. Med. Res.285-289.
11. Sriram (2007) "Steroids", Medicinal chemistry Pearson Education. India. 437.
12. Hartgens F, Van Marken, Lichtenbelt WD, Ebbing S, Vollaard N, Rietjens G, Kuipers H (2001) Body composition and anthropometry in body builders regional changes due to nandrolone decanoate administration .Int. J. Sports Med., 22(3): 235-41.
13. Mulligan K, Zackin R, Clark RA, Alston-Smith B, Liu T (2005) Effect of nandrolone decanoate therapy on weight and lean body mass in HIV-infected women with weight loss: a randomized, double-blind, placebo-controlled, multicenter trial. Arch. Int. Med., 165: 578–585.
14. Johansen KL, Painter PL, Sakkas GK, Gordon P, Doyle J, Shubert T (2006) Effect of resistance exercise training and nandrolone decanoate on body composition and muscle function among patients who receive hemodialysis: a randomized, controlled trial, J. Soc Nephrol., 17(8): 2307-2314.
15. Frisoli A Jr, Chaves PH, Pinheiro MM, Szejnfeld VL (2005) The effect nandrolone decanoate on bone mineral densimuscle mass, and hemoglobin levels in elderly women with osteoporosis: a double-blind, randomized, placebo- controlled clinical trial .J. Gerontol. A. Biol. Med. Sci., 60(5):648-53.
16. Saha B, Rajadhyaksha GC, Ray Sk (2009) Beneficial effect of nandrolone decanote in wasting associated with HIV. J. Indian. Med. Assoc., 107(5):295-9.
17. Yarrow JF, Conover CF, McCoy SC, Lipinska JA, Santillana CA, Hance JM (2011) 17 beta-hydroxyestra-4,9,11-trien-3-one (trenbolone) exhibits tissue selective anabolic activity : effect on muscle, bone, adiposity, hemoglobin, and prostate, Am .J. Physiology .Endocrinal. Metab. 300 (4): 650-60.
18. Schwingel PR, Cotrim HP, Salles BR, Almeida CE dos, Santos CL, Nachef B (2011) Anabolic-androgenic steroids: a possible new risk factor of toxicant- associated fatty liver disease. Liver Int., 31(3): 348-53.
19. Frankenfeld SP, de Oliveira, LP Ignacio, DL Coelho, RG Mattos, MN Ferreira AC (2014) Nandrolone decanoate inhibits gluconeogenesis and decreases fasting glucose in Wistar male rats .J. Endocrinol.,220 (2):143–53.
20. Johnson RDO, Connor ML, Kerr RM (1995) Extreme serum deviations of aspartate aminotransferase Am .J, Gastroenterology, 90:5-244.
21. Tietz NW (1999) Text book of clinical chemistry. 3nd Ed .C.A. Burtis, E.R. Ashwood, W.B. Saunders. 652-1431.
22. Walter M, Gerard H, Microchem M (1980) 15, 231.
23. West JB (1985) Physiological basis of medical practice. 11th ed, Williams and Wilkins, Baltimore. 418-425.
24. Doumas BT, Watson WA, Biggs HG (1971) Albumin standard and the measurement of serum albumin with bromcroesol green. Clin. Chem. Acta., 31: 87-95.
25. Labbe D (1996) Am. Biol. Clin., 285-298.
26. Bancroft JD, Stevens A (1982) Theory and practice of histological techniques 2nd ed . Churchill Livingstone .XIV+ 647. Am. Fam. Physician., 54(3):986-992.
27. Morgan GA, Leech NA, Gloecner GW, Barrett KC (2010) SPSS for introductory statistic: use and interpretation .2nd ed . Lawrenz Erlbaum associatiates, publishers Mahwah, New Jersey. London.
28. Shahraki MR, Mirshekari H, Shahraki AR (2015) Chronic high doses of Nandrolone Decanoate on blood cell, lipoprotein profile, and liver enzymes in male rats. Zahedan. J. Res.Med. Sci., 7365.

29. Mohammed ARS, Al-Galad GM, Abd- Elgayd AA, Mwaheb MA, Elhanbuli HM (2017) Effect of Nandrolone Decanoate (Anabolic steroid) on the liver and kdney of male albino rats and the role of antioxidant (Antox-Silymarin) as adjuvant therapy, J. Drug. Metabol. Toxicol, 8(1): 224.

30. Guyton MD, Hall PhD (2006) Textbook of medical physiology, 11th ed., 1003-1006.

31. Joumaa WH, Leoty C (2001) Differential effects of nandrolone decanoate in fast and slow rat skeletal muscles. Med. Sci. Sports. Exerc.,33(3):397–403.

32. Lindqvist AS, Fanlike C (2005) Nandrolone decanoate has long-term effects on dominance in a competitive situation in male rats. Physiol. Behav. 84(1):45–51.

33. Shahraki MR, Rafeei R (2015) The effects of sub acute Supraphysiological dose of Nandrolone Decanoate on liver enzymes and lipid profiles in rats. Zahedan. J. Res.Med. Sci., 17(9):9045.

34. Fontana K, Campos GE, Staron RS, da Cruz-Hofling MA (2013) Effects of anabolic steroids and high-intensity aerobic exercise on skeletal muscle of transgenic mice. PLoS. One. 8(11).

35. Gold J, High HA, Li Y, Michelmore H, Bodsworth NJ, Finlayson R (1996) Safety and efficacy of nandrolone decanoate for treatment of wasting in patients with HIV infection. AIDS. 10(7):745–52.

36. Fortunato RS, Marassi MP, Chaves EA, Nascimento JH, Rosenthal D, Carvalho DP (2006) Chronic administration of anabolic androgenic steroid alters murine thyroid function. Med. Sci. Sports Exerc.,38(2):256–61.

37. Kuipers H, Wijnen JA, Hartgens F, Willems SM (1991) Influence of anabolic steroids on body composition, blood pressure, lipid profile and liver functions in body builders, Int .J. Sports .Med.,12(4):413–8.

38. Gold J, MJ Batterham, H Rekers, MK Harms (2006) Effect of nandrolone decanoate compared with placebo testosterone on HIV-associated wasting. HIV Med., 7(3): 146-155.

39. Sardar P, Jha A, Roy D, Majumdar U, Guha P, Roy S, Banerjee R, Banerjee AK, Bandyopadhyay D (2010) Therapeutic effects of nandrolone and testosterone in adult male HIV patients with AIDS wasting syndrome (AWS): a randomized, double-blind, placebo-controlled trial. HIV Clinical .Trials. 11(4): 220-229.

40. Schols AM, PB Soeters, R Mostert (1995) Physiologic effects of nutritional support and anabolic steroids in patients with chronic obstructive pulmonary disease. A placebo controlled randomized trial. Am. J. Respir. Crit. Care. Meal. 152: 1268-1274.

41. Rocha FL, Carmo EC, Roque FR, Hashimoto NY, Roque FR, Rossoni C, Aneas I, Negrao CE, Krieger JE, Oliveira EM (2007) Anabolic steroids induce cardiac renin angiotensin system and impair the beneficial effects of aerobic training in rats. Am. J. Physiol. Heart. Circulat. Physiol., 293(6): 3575-3583.

42. Fineschi V, Dl Paolo, M Neri, M Bello, S D'Errico, S Dinucci, D Parente, R Pomara, C Rabozzi, R Riezzo, RI Turillazzi (2011) Anabolic steroids and exercise-induced cardio-depresant cytokines and myocardial ß(1) receptor expression in CD1 mice. Current. Pharmaceut. Biotechnol., 12(2): 275-84.

43. Pertusi R, Dickerman RD, McConathy WJ (2001) Evaluation of aminotransferase elevations in a bodybuilder using anabolic steroids: hepatitis orrhabdomyolysis. J Am. Osteopath Assoc., 101 (7):391–4.

44. Borsari M, Gabbi C, Ghelfi F, Grandi R, Saladini M (2001) Silybin, a new iron-chelating agent. J. Inorg .Biochem., 85:123-129.

45. Gerez JR, Frei F, Cristina L, Camargo C (2005).Histological assessment of ovaries and uterus of rats subjected to Nandrolone Decanoate treatment .Contraception.27:77-80.

46. Tasgin E, Haliloglu S (2013) The Administration of nandrolone decanoate may cause multiple organ failure. Sci .Movement .Health. 13: 784-788.

47. Minkin DM, Meyer ME, Van Haaren F (1993) Behavioral effects of long term administration of an anabolic steroid in intact and castrated male Wistar rats. Pharmacol. Biochem. Behave. 44: 959-963.

48. Hoseini L, Roozbeh J, Sagheb M, Karbalaydoust S, Noorfshan A (2009) Nandrolone Decanoate increases the volume but not the length of the proximal and distal convoluted tubules of the mouse kidney.Micron., 40: 226-230.

49. Boada LD, Zumbado M, Torres S (1999) Evaluation of acute and chronic hepatotoxic effects exerted by anabolic-androgenic steroid stanozolol in adult male rats. Arch .Toxicol.73:465–72.

50. Van Amsterdam J, Opperhuizen A, Hartgens F (2010) Adverse health effects of anabolic-androgenic steroids. Regul. Toxicol. Pharmacol. 57(1):117–23.

51. Neri M, Bello S, Bonsignore A, Cantatore S, Riezzo I, Turillazzi E (2011) Anabolic androgenic steroids abuse and liver toxicity. Mini .Rev. Med. Chem., 11(5):430–7.

52. Acharjee BK, Mahanta R, Borkotoky A (2010) Nandrolone decanoate enhances the activities of cholanthrene-induced glutathione-s-transferase in liver tissue of albino mice. Drug. Metab. Lett., 4(1):1–6.

53. Uskokovic-Marcovic S, Milencovic M, Topic A, Kotur-Stivuljevic J, Stefanovic A, Antic-Stancovic J (2007) Protective effect of tungstophoric acid and sodium tungstate on chemically induced liver necrosis in wistar rats. J. Pharm. Phamaceut Sci., 10(3): 340-349.

54. El Saeed TA, Eman Taha, M Hassan, MS Amany (2012) Modulatory effects of Artichoke leave extract Nandrolone Decanoate-induced biochemical alterations in rats. Global J. Biotech. Biochem. 7(2): 68-78.

55. Wolker K, Edward C (1999) Clinical pharmacy and Therapeut. S .2nd ed Churchill Living Stone. 51.

56. Temme EH, Zhang J, Schouten EG, Kesteloot H (2001) Serum bilirubin and 10-year mortality risk in a Belgian population. Can. Caus. Cont., 12(10): 887-894.

57. Sullivan ML, CM Martinez, P Gennis, EJ Gallagher (1998) The cardiac toxicity of anabolic steroids. Prog. Cardiovascular. Dis., 41: 1-1.

58. Venancio DP, Nobrega AC, L Mello, ST M (2010) Avaliacao descriptive sobre o use de steroids anabolizantes e seu efeito sobre as variaveis bioquimicas eneuro endocrines is individual's que practicum exercise resisted. Revista .Brasileira de. Medicines do .Sported. 16(3): 191-195.

59. Salih NA (2015) Effect of nettle (*Urtica dioica*) extract on gentamicin induced nephrotoxicity in male rabbit's .Asian Pac .J. Trop .Biomed. 5(9): 756-760.

60. Nenad SM, Dragan V Slavimir (2008) Glomerular basement membrane alterations induced by gentamicin administrations in rats. Experimental. Toxicological. Pathol, 60: 69-75.

61. Karbalay-Doust S, Noorafshan (2009) "Stereological study of the effects of ND on the mouse liver". Micron, 40:471-475.

62. Markova MS, Zeskand J, McEntee B, Rothstein J, Jimenez SA, Siracusa LA (2004) Role for the androgen receptor in collagen content of the skin. J. Invest .Dermatol. 123(6):1052–6.

63. Takashashi M, Tatsugi Y, Kohno T (2004) "Endocrinological and pathological effects of anabolic-androgenic steroid in male rats". Endocrine J., 51(4): 425-434.

64. Bento-Silva MT, Martins MDCDCE, Torres-Leal FL, Barros TL, Carvalho ILDNFD (2010) Effects of administering testosterone undecanoate in rats subjected to physical exercise: effects on the estrous cycle, motor behavior and morphology of the liver and kidney. Braz. J. Pharm. Sci., 46: 79-89.

65. Shabir N, Malik H, Sajjad S, Abbas MN (2015) Effect of Nandrolone Decanoate, Boldenone Undecylenate on Renal Status of Rabbits. Global Veterinarian. 14: 432-438.

