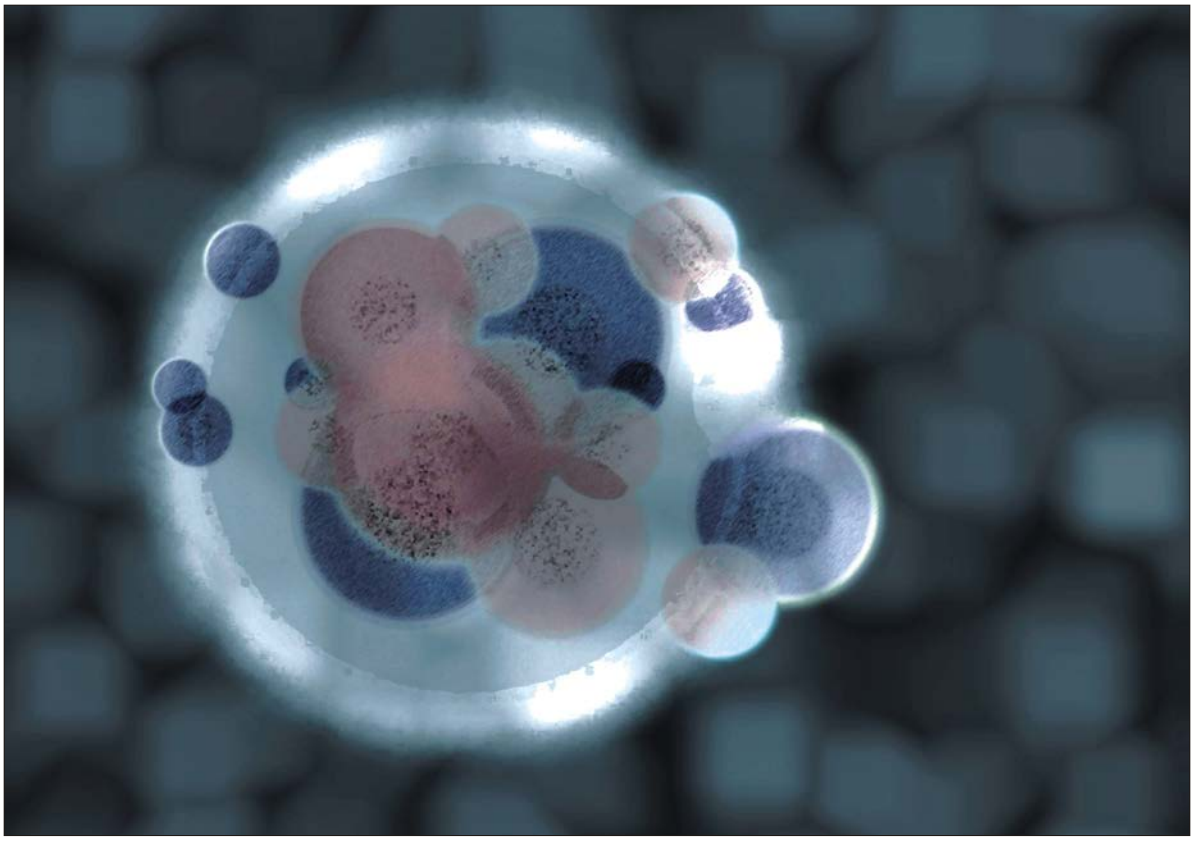

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Histopathological Evidences of the Nephritic PathologicalAlterationsInduced by the Anabolic Androgenic Drug (Sustanon) in Male Guinea Pigs (*Cavia porcellus*)

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Abstract: The present histopathological study on male guinea pigs aims to investigate the potential histopathological alterations and damages in the kidneys structure induced by the repeated administration of two doses of Sustanon drug. The treated animals in this study were injected once every week with two Sustanon doses as follow (15 mg kg^{-1} in group GII and 30 mg kg^{-1} in group GIII) for a continuous treatment period of 6 weeks. The histopathological examination of the of kidneys cross sections of the treated animals in group (GIII) showed multiple abnormal alterations and damages in the kidneys in the following forms glomeruli atrophy and glomeruli fragmentation accompanied with dilatation of the urinary spaces, abnormal vasodilatation of blood vessels, irregular dilatations of the proximal and distal convoluted tubules associated with degeneration of epithelial cells in the tubules lumens. Furthermore, the worst histopathological damages induced by Sustanon doses appeared in the form of massive and intensive blood hemorrhage in different places of the nephritic tissues, severe rupture of walls of the proximal and distal convoluted tubules and wide abnormal lacerations inside the nephritic tissues. These results may prove that abusing high doses of Sustanon for long periods by athletes can cause severe histopathological damages in the kidneys structure. One of important points which can be concluded from the current results is that physicians should take renal disorders in mind seriously as one of the predictable complications resulting from abusing these drugs such as Sustanon. Finally, the present study recommends that athletes and youths should be supplied with much more medical enlightenment about the health risks and the complications which resulted from abusing these drugs through media.

Key words: Sustanon, anabolic androgenic drugs, abuse, nephritic, histopathological damages

INTRODUCTION

The phenomenon of abusing anabolic androgenic drugs by many youths and athletes is a serious health phenomenon which increased rapidly in recent years. To realize how this phenomenon is widespread, we should know that this risky phenomenon have been confirmed and documented in clinical cases reports by number of investigators in many countries around the world including : U.K, Germany, Australia USA, Canada, Japan, China and even in some Arab countries (Yesalis, 2000; Hausmann, 1998; Fitch, 2008; Tahtamouni *et al*., 2008). Unfortunately, many of the athletes, specially in the power sports and the youths abuse illegally high doses of these anabolic androgenic drugs such as deca-durabolin, metandienone, stanozolo, oxandrolone, oxymetholone and sustanon, in order to obtain and produce a rapid and huge increasing in the skeletal muscles mass and to improve their performance during the sport competitions, i.e., these drugs are abused to act as a performance-enhancing drugs (Karch, 1997; Lenehan, 2003; Hausmann, 1998). However, in regard the existence of this problem in the Arab countries, the recent field study of Tahtamouni *et al.* (2008) in Jordan provided a strong evidence proving the existence of this risky phenomenon in Jordan and other Arab countries as well. According to this field study, it was found that the percentage of the abusers among the colleges students samples was 4.2%, whereas the percentage of the abusers among the athletes samples was found 26%, most of them were abusers for long periods, the ages of the abusers were found between 19-28 years old. The study reported that the abusers obtained the information about where and how to get these drugs from their friends and coaches. In addition, the study reported also that due to the absence of sufficient official restrictions in most Arab countries on these drugs, it was very easily for the abusers to obtain these drugs directly from the pharmacies. On the other hand, it is very important in fact to mention that these anabolic androgenic drugs such as Sustanon and deca-durabolin are actually a useful medical drugs which possess multiple clinical therapeutic benefits (Monaghan, 2001; Harvey and Champe, 2002; Karila, 2003). For instance, Sustanon is one of these anabolic drugs which

has many useful therapeutic usages, it is clinically used to treat cases of osteoporosis, eunuchoidism, male hypogonadism and infertility, absence of male libido (Harvey and Champe, 2002; Karila, 2003; Lenehan, 2003). In regard Sustanon, it is characterized by a very unique and distinguish pharmacological structure and properties comparing to the other anabolic drugs, as it consists of an oily mixture of four different testosterone ester compounds which provides a continues release of testosterone into the blood plasma producing a stable testosterone level in the blood serum for long durations extend to 3-4 weeks (Monaghan, 2001; Beotra, 2005). This distinguish properties of Sustanon increase its anabolic effectiveness period, therefore, Sustanon is described as long acting anabolic androgenic steroid (Wills, 2005). These special pharmacological properties of Sustanon, specially the long acting effectiveness, can explain why Sustanon is more attractive to be abused by the athletes (Hartgen and Kuipers, 2004). Overall, previous studies reported many serious adverse effects resulted from abusing these anabolic drugs which include: cardiovascular disorders (particularly enlargement of the left ventricle) which can lead to sudden cardiac death, acute hepatitis and jaundice, testicular dysfunction which can lead to infertility, hypertension, behavioral disorders in the form of sexual over-stimulation and high increase in the aggressiveness (Stimac *et al*., 2002; Socas *et al*., 2005; Fineschi *et al*., 2007). By reviewing the literature, it was noticed that the hepatic and cardiovascular histological damages induced by abusing these drugs have been well studied and documented by Yesalis (2000), Stimac *et al*. (2002) and Kindermann (2006). While in contrary, very limited studies are available about the potential nephritic histopathological alterations induced by abusing these drugs. For example, Hartung *et al*. (2001) study is one of the very few studies which investigated the abnormal kidney histological changes induced by deca-durabolin abuse. The study documented a case report of nephritic damages and serious renal disorders in 27 years old body builders who abused high doses of Deca-Durabolin (750-1000 mg week^{-1}) for 10 week. According to this study, the kidney biopsy of this abuser patient revealed the following nephritic histopathological alterations: nephrosclerosis accompanied with obstructive lesions of preglomerular vessels, glomerulosclerosis and diffuse tubulo-interstitial damages. But unfortunately, in regard the Sustanon abuse in particular, no previous studies have attempted to investigate the potential nephritic histopathological changes which may result from abusing it for long periods by athletes. The study of Modlinski and Fields (2006) indicated that because the abuse of these anabolic androgenic drugs is elicited and occurred secretly among the athletes, most of our knowledge about the adverse effects of these drugs is obtained mainly from the clinical cases reports which reached the hospitals in some countries, therefore, some of these adverse effects such as the nephritic histopathological changes are still very limited. Therefore, the importance of the present study comes from the lack of sufficient information about the potential nephritic histopathological alterations which may result from Sustanon abuse, as it is one of the prior studies which explored the negative effects of Sustanon abuse in particular on the kidneys structure. The aim of current study on male Guinea pigs were to investigate the potential nephritic histopathological damages induced by repeated administration of two doses of Sustanon for a treatment period of 6 weeks.

MATERIALS AND METHODS

The present study have been carried out in May-June 2008 in King Fahed medical research center, King Abdull Aziz university, Jeddah, Saudi Arabia.

Sustanon doses: Sustanon 250 ampoules (manufactured by N. V Organon Oss Inc. Holland) have been obtained from the local pharmacies in Jeddah city, Saudi Arabia. Each ampoule contain 1 mL of oily solution of Sustanon 250. According to the manufacturer this 1ml of Sustanon 250 consists of the following four different testosterone ester compounds: Testosterone propionate, Testosterone phenylprpropionate, Testosterone isocaproate and Testosterone decanoate. Therefore, in the present study two tested doses of Sustanon 250 have been selected (15 and 30 mg kg^{-1} of the animal body weight) based on the previous studies of Segura *et al*. (2000) and Johansson *et al*. (2002) which were performed also on guinea pigs. These two tested doses are believed to simulate experimentally the cases of sustanon abuse in the athletes. The method used to prepare these two tested doses was as that used by Segura *et al*. (2000) study.

Experimental animals and treatment: Twenty four adult male Guinea pigs (*Cavia porcellus*) (Dunkin Hartely strain) weighing 700-750 g were used in the present study, the animals have been obtained from the animal house unit of King Fahed Medical Research Center in King Abdul Aziz University in Jeddah. Each animal was housed in a wide proper plastic cage and kept under constant normal temperature (22°C), 12 h dark/light cycle (Al-Tayib, 2004). Distilled water and diet were provided daily. Prior the experiment start, animals were left for two weeks to acclimatize. After these acclimatization period, animals were divided in-to 3 groups (8 animals in each),

the first group (GI) was the control group, whereas the second group (GII) and the third group (GIII) were the treated groups. In these two treated groups (GII) and (G III) each animal was injected intramuscularly (i.m.) once every week with a single dose of (15 and 30 mg kg^{-1}, respectively), this pattern of treatment was continued for a treatment period of 6 weeks.

Preparation of the histological sections: At the end of the treatment period, each animal of the three groups was anesthetized by inhalation of drops of diethyl ether in a piece of cotton, then kidney samples were immediately collected within few minutes and fixed in buffer formalin solution. Kidney samples were collected from the two treated groups (GII and GIII) and control group (GI). The routine histological preparation steps were performed which include: dehydration, embedding, sectioning and staining with Hematoxyline and Eosin stains according to the method of Culling (1974). Kidneys cross sections were examined under the light microscope to determine and monitor any histopathological damages in kidney tissues.

RESULTS AND DISCUSSION

Histopathological examination

Control group: As shown in Fig. 1, the histological examination of kidneys cross sections of the control animals showed normal and regular histological structure, the kidney consists histologically of two layers cortex and medulla, the nephrons appeared in their normal shape, Bowman capsule appeared in its normal round regular shape containing the glomerulus and urinary space as shown in Fig. 1a. Proximal convoluted tubules appeared close to Bowman capsules with their narrow regular lumens, while distal convoluted tubules appeared with their normal wide lumens (Fig. 1b).

Treated groups

Effects of 15 mg kg^{-1} dose in group: (GII) As shown in Fig. 2, limited histopathlogical alterations were observed in the kidneys cross sections of the animals treated with dose. The observed abnormal alterations appeared in the two following forms: fragmentation of glomeruli accompanied with the appearance of vacuolated lumens in the proximal tubule and distal tubule (Fig. 2a), as well as vasodilatations of some blood vessel in the nephritic tissue (Fig. 2b). These observed results indicated the ability of abusing this Sustanon dose for long periods more than 8 weeks to produce more serious histopathological damages in the kidneys.

Effects of 30 mg kg^{-1} dose in group (GIII): The treatment with this Sustanon dose for 8 weeks induced very serious histopathological damages in the kidneys structure. These observed nephritic damages proved the occurrence of massive pathological injuries in the kidneys

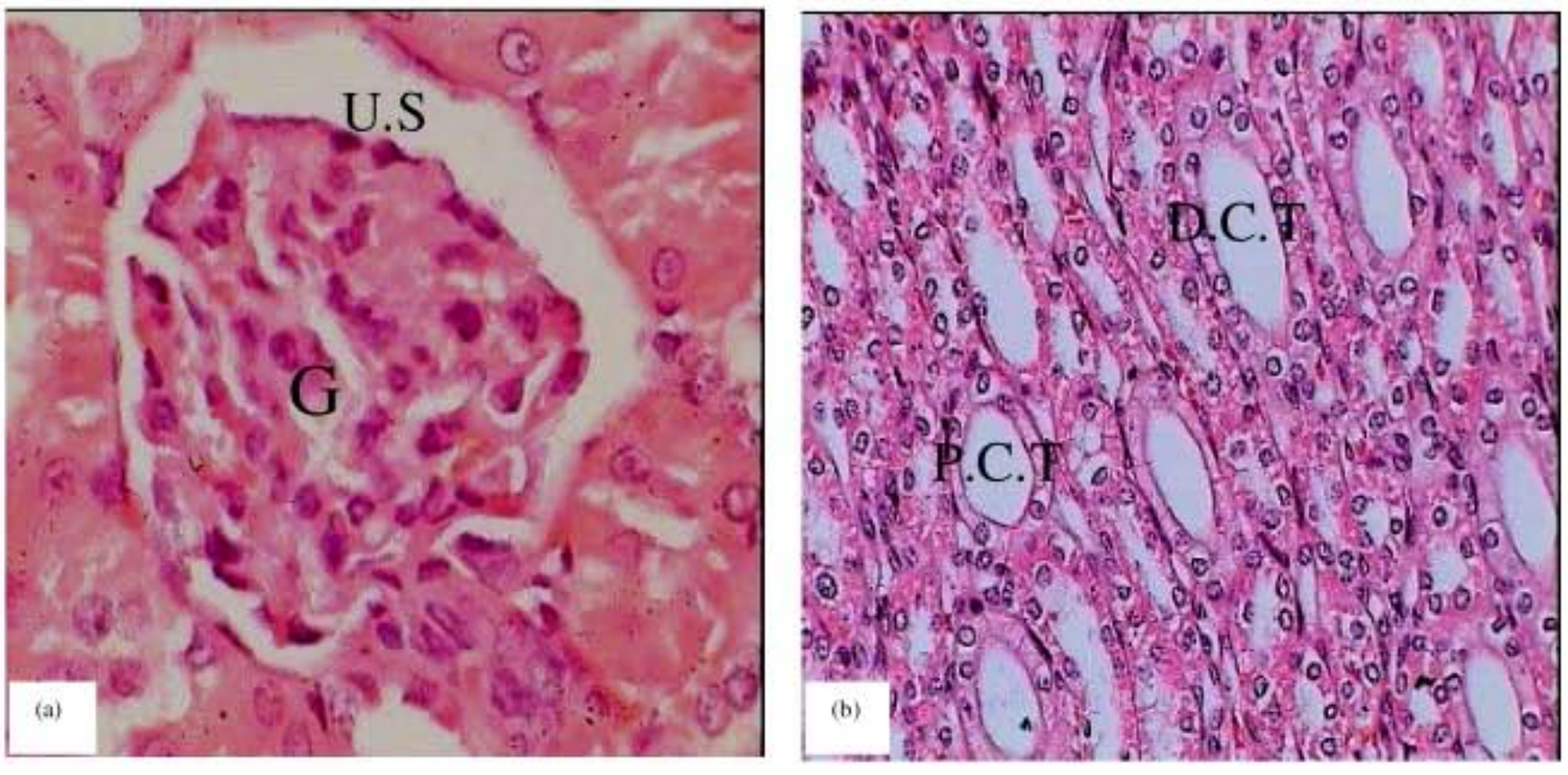

Fig. 1: (a) Light micrograph of guinea pig kidney cross section (c.s.) of control group (GI), shows normal shape of the nephritic glomerulus (G) inside the urinary space (U.S.), notice there is no presence of any abnormal alterations such as glomerulus atrophy or fragmentation (x1000, H and E stains). (b) Kidney cross section (c.s.) of control animal, shows normal and regular shape of the proximal convoluted tubules (P.C.T.) and distal convoluted tubules (D.C.T.), notice the absence of any histopathological alteration such as tubular dilatations or tubular walls rupture, also no blood hemorrhage between the tubules. (x400, H and E stains)

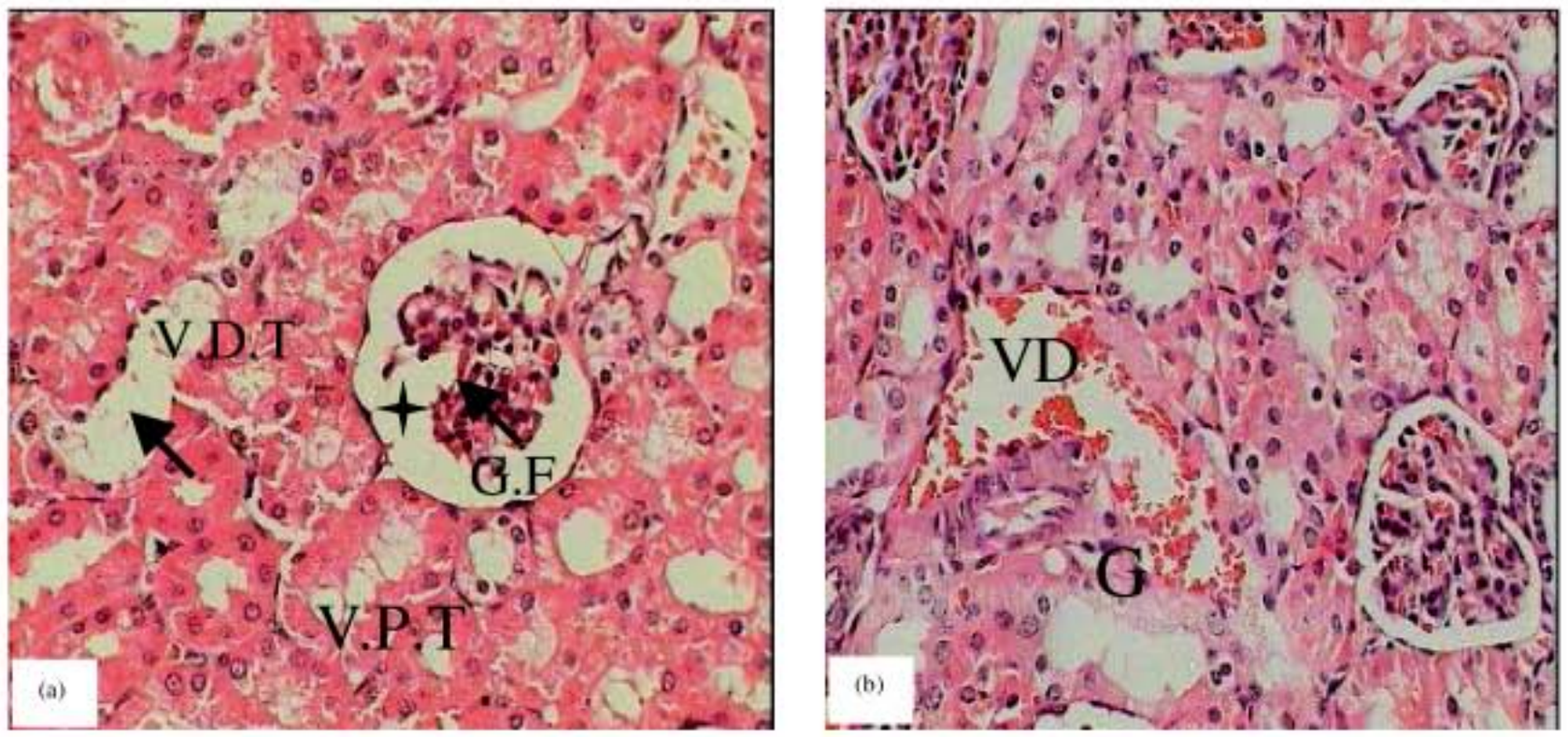

Fig. 2: (a) Light micrograph of kidney (c.s.) of animal treated with 15 mg kg^{-1} dose for 6 weeks (group G II), shows fragmentation of glomerulus (G.F.) (star) accompanied with the presence of vacuolated lumens of the proximal tubule (V.P.T.) (arrow) and the distal tubule (V.D.T.) (arrow). (x400, H and E stains). (b) Kidney (c.s.) of animal treated with the dose of 15 mg kg^{-1}. (group G II) for 6weeks, observes the abnormal vasodilatation (VD) and the irregular shape of one of the blood vessel nearby the glomeruli (G). (x400, H and E stains)

histological structure as a result of long term treatment with this Sustanon dose. These observed nephritic histopathological damages appeared in different various patterns including:- glomeruli fragmentation and glomeruli atrophy as shown in Fig. 3a-d, the fragmented glomeruli appeared with hyalinized capillaries and red blood cells leakage out side the glomeruli capillaries to the urinary spaces (Fig. 3a, 4a, b), while the atrophied glomeruli appeared with shrunken capillaries and surrounded by dilated urinary spaces (Fig. 3c, d). Furthermore, the worst histopathological damages appeared in the form of intensive and massive blood hemorrhage in many places inside the nephritic tissues accompanied with vasodilatation of some blood vessels shown in Fig. 4a-d, this intensive blood hemorrhage was observed close to damaged glomeruli (Fig. 4a) and between the distal convoluted tubules (Fig. 4d), the blood hemorrhage appeared also inside Bowman s capsules in the glomeruli (Fig. 4a, b, 5a), many red blood cells appeared in the outside out side the blood vessels of the glomeruli urinary space. In addition, abnormal dilatations and irregular shapes were observed in many distal convoluted tubules as shown in Fig. 5b and c as well as in few proximal convoluted tubules (Fig. 5a), these abnormal tubular dilatations were accompanied with degeneration and lysis of the epithelial cells laying the walls of these damaged tubules as shown in Fig. 5b-d. Some of these dilated tubules appeared in a very abnormal irregular shapes as shown in Fig. 6a-d. On the other hand, some of the dilated proximal and distal convoluted tubules appeared with lumens contained large number of empty vacuoles (vacuolated tubules) (Fig. 6b). In addition, the examination revealed the occurrence of severe rupture of the walls of some proximal and distal tubules as shown in Fig. 6c, d, the tubular walls rupture is considered as a serious form of the nephritic damages.

In addition, there was another severe damage observed in kidney cross sections which was in the form of wide lacerations inside the nephritic tissue in different places as shown in Fig. 7a-d. Therefore, It can be concluded from these serious observed damages that abusing high doses of the anabolic androgenic drug (Sustanon) for long periods by athletes can cause wide destruction of the normal kidneys structure, which may lead to produce serious renal disorders such as renal failure in late stages.

It is important at the beginning to mention that abusing anabolic androgenic drugs such as Sustanon and Deca-Durabolin by athletes and youths is very risky phenomenon, as according to previous clinical studies and cases reports, many athletes and youths abusers lost their live by sudden cardiac attacks due to abusing high doses of these drugs (Urhausen *et al*., 2004; Fineschi *et al*., 2007). Hence, new studies appear yearly providing more and more evidences about the multiple adverse effects and the complications of abusing these drugs which can threaten the live of the abusers. Moreover, to realize how serious this health problem is,

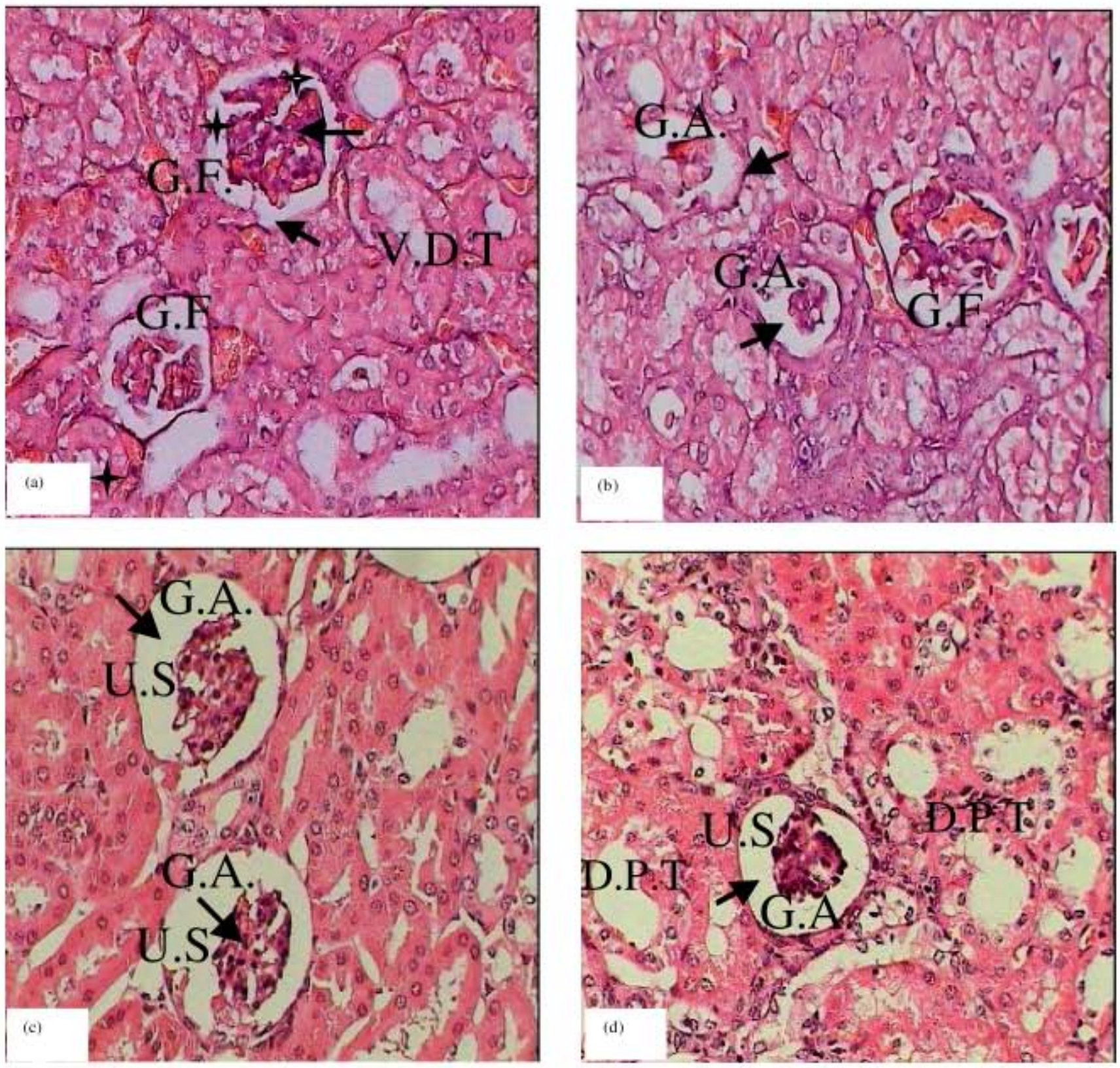

Fig. 3: (a) Light micrograph of guinea pig kidney cross section (c.s.) treated with 30 mg kg^{-1} dose for 6 weeks (group GIII), shows fragmentation of two glomeruli (G.F.) (stars), also notice the presence of RBCs leakage from the glomeruli capillaries (arrows) (x400, H and E stains). (b) Kidney cross section (c.s.) treated with 30 mg kg^{-1} dose for 6 weeks (group G III), shows glomerulus fragmentation (G.F.) and glomeruli atrophy (G.A) (arrows), also notice the presence of RBCs leakage inside the fragmented glomerulus (x400). (c-d) Kidney cross sections from the same group (GIII) reveals glomeruli atrophy (G.A) (arrows) with dilatation of urinary spaces (U.S.), also note dilatation of proximal tubules (D.P.T.), (x400)

we have to know that governments in some countries spent millions to stand against this phenomenon, for example, in U.S.A a great institute has been established to face this problem called (the association against steroids abuse) which provide free online medical information to the public regarding the health hazards of abusing these drugs (Ryan and Richard, 2005; Wills, 2005). On the other hand, number of factors are believed to be responsible for the continuation of this risky phenomenon. For instance, according to the field study of Tahtamouni *et al.* (2008), it is believed that one of these factors is the wrong belief among the athletes and youths abusers that the adverse effects of these drugs are reversible effects and it can be medically treated easily after the sport competitions. In fact, this belief is absolutely not correct as number of previous studies proved that such abuse can cause in many cases irreversible serious adverse effects such as the cardiac disorders and chronic hepatitis (Kennedy and Lawrence, 1993; Stimac *et al.*, 2002; Fineschi *et al.*, 2007). In addition, the absence of official and medical restrictions on the pharmacies which sell these drugs without prescriptions in many countries of the third world is also

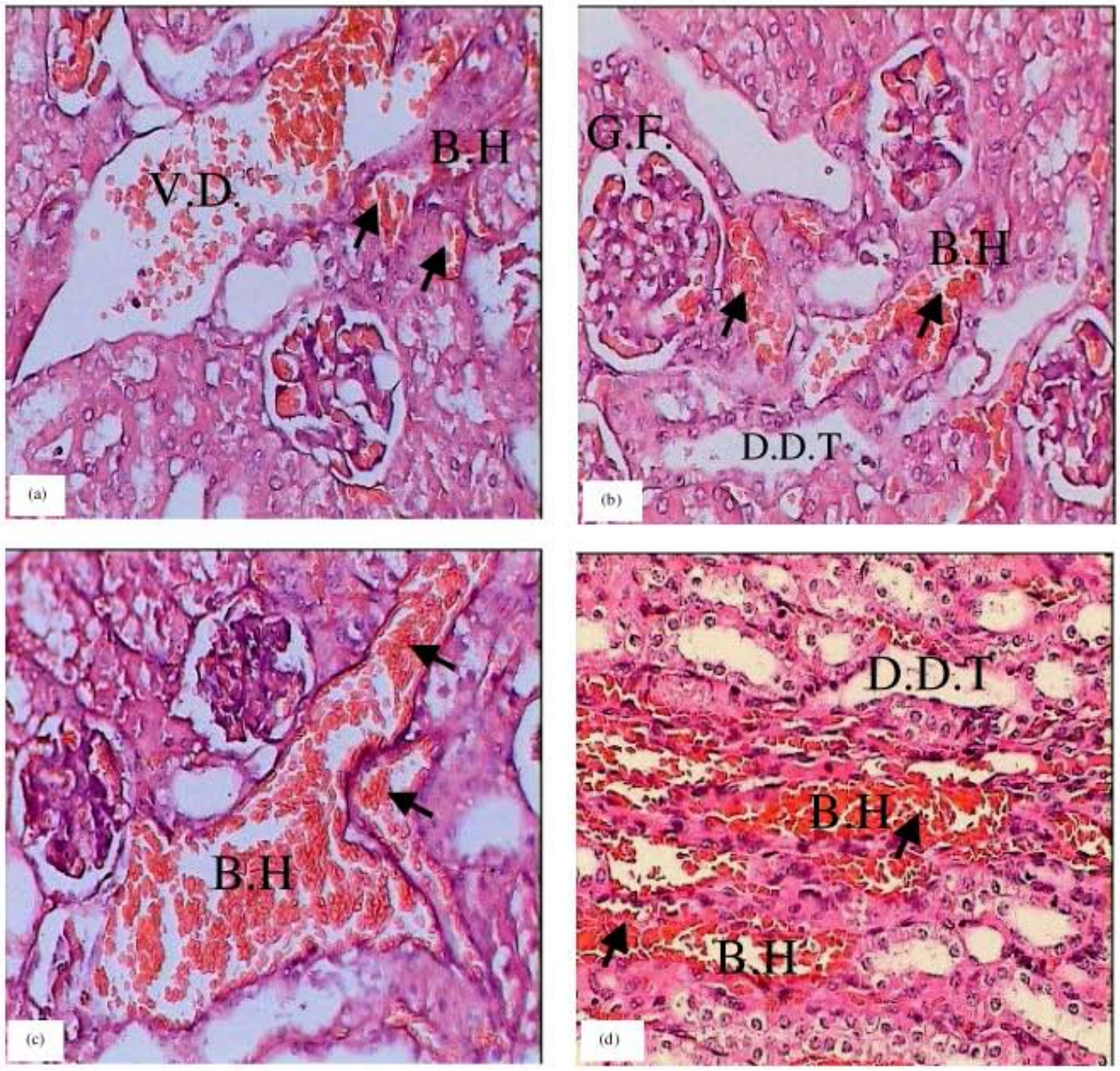

Fig. 4: (a) Light micrograph of kidney cross section (c.s.) of animal treated with 30 mg kg^{-1} dose for 6 weeks (group G III), illustrates the presence of abnormal and irregular vasodilatation of a blood vessel (VD.) beside Bowman s capsule, also notice the blood hemorrhage inside the tissue (B.H) (arrows) (x400, H and E stains). (b) Kidney cross section of animal of group (GIII) shows blood hemorrhage (B.H) (arrows). in many places inside the tissue, also notice the glomeruli fragmentations (G.F.) accompanied with RBCs leakage from the glomeruli capillaries and abnormal dilatation of the distal convoluted tubules (D.D.T) (x400). (c) Kidney (c.s.) of treated animal of group (G III), reveals wide and intensive blood hemorrhage (B.H) (arrows) out side glomeruli, also notice the irregular vasodilatation of one of the blood vessel. (x400). (d) Kidney (c.s.) from the same group (G III), shows massive and multiple blood hemorrhage (B.H.) (arrows) between the dilated distal tubules (D.D.T.). (x400, H and E stains)

another main factor responsible for the continuation of this problem (Monaghan, 2001; Tahtamouni *et al*., 2008). However, by reviewing the literature of Sustanon abuse in particular, the present study is believed to be as far as we know one of the prior histological studies which investigated the potential adverse effects of the repeated administrations of Sustanon doses for long periods which is similar to abuse cases on the kidneys normal histological structure. Although, some investigators reported that the adverse effects of anabolic androgenic drugs abuse on the kidneys are very rare (Yesalis, 2000; Harvey and Champe, 2002), the present results provided a strong evidences about the potential nephritic damages which can be induced by Sustanon abuse. Overall, comparing to the previous studies which were performed on other anabolic androgenic drugs, it seem that the present results support the previous study of Zeier *et al*. (1998) which reported that abusing certain types of these

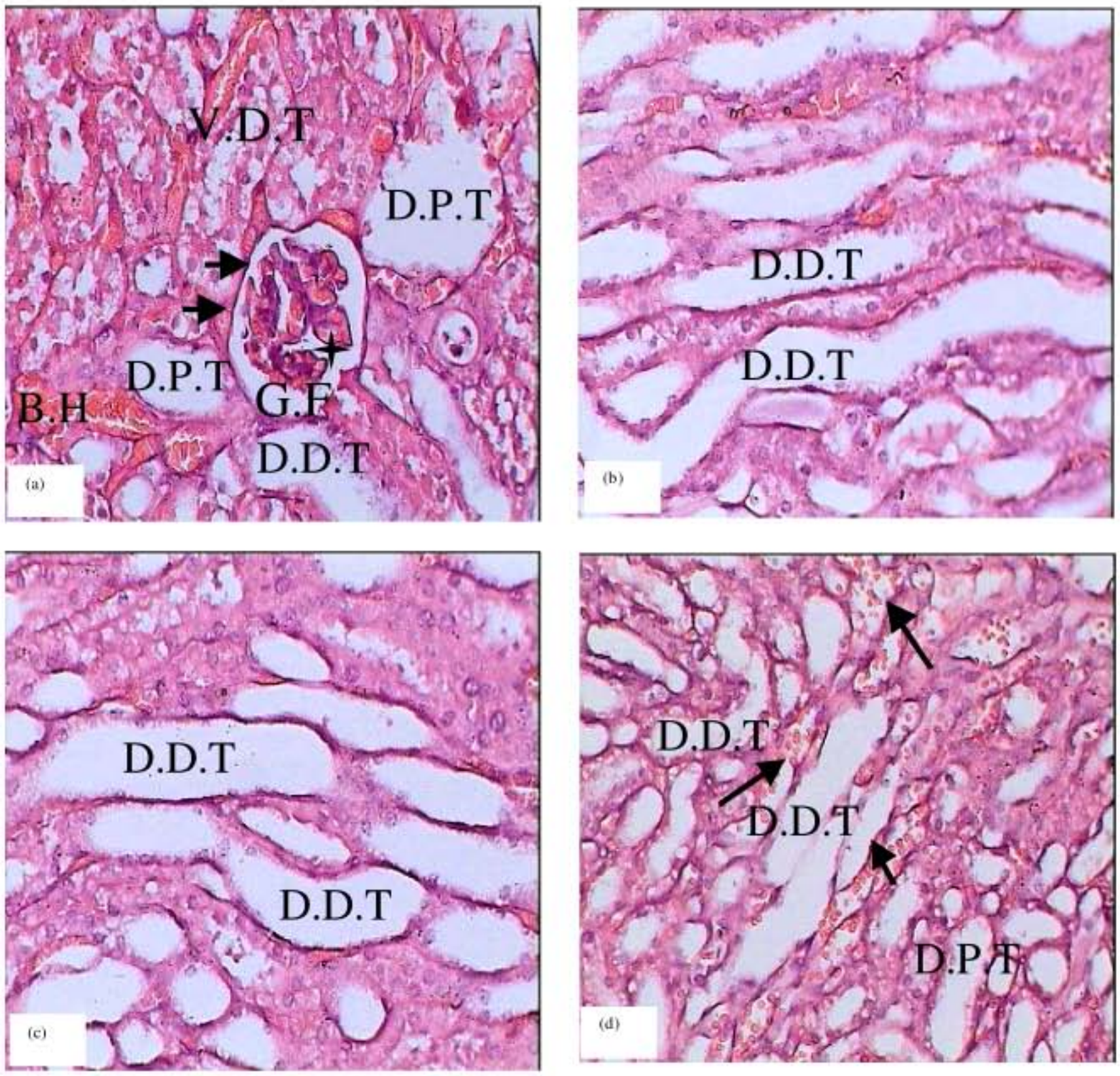

Fig. 5: (a) Light micrograph of kidney cross section (c.s.) of animal treated with 30 mg kg^{-1} dose for 6 weeks (group GIII), shows abnormal dilatation of proximal convoluted tubule (D.P.T.) and dilated distal tubules (D.D.T) beside fragmented Glomerulus (G.F.) (star) which contained RBCs leakage, also observes the presence of vacuolated distal tubules (V.D.T) (arrows) and blood hemorrhage (B.H) inside the tissue. (x400, H and E stains). (b-c) Two kidney (c.s.) from that same treated group G III, shows abnormal dilatation and irregular shapes of many distal convoluted tubules (D.D.T) associated with degeneration of the epithelial cells laying the walls of these tubules. (x400). (d) Kidney (c.s.) of treated animal of group GIII, represents also dilatation of both distal tubules (D.D.T.) and the proximal tubules (D.P.T.), also notice the blood hemorrhage (arrows) between the tubules. (x400, H and E stains)

drugs caused abnormal histological changes in the kidneys in the form of glomeruli atrophy and dilatation of distal tubules in rats. Similarly, the present results correspond also with the previous study of Habscheid *et al.* (1999) which documented a case of acute renal failure associated with hepatitis and cholestasis in 28 years old athlete abuser who consumed high doses of two anabolic androgenic drugs for several months. Moreover, the current histopatholigical findings support the observations of Hartung *et al.* (2001) study which documented a severe nephritic alterations in body builder who abused high doses of Deca-Durabolin for 10 week. According to this study, the kidney biopsy examination of this abuser revealed the following nephritic damages: nephrosclerosis, obstructive lesions of preglomerular vessels, glomerulosclerosis and diffuse tubulo-interstitial damages. Furthermore, the present results seem to match with Hoseini *et al.* (2009) study

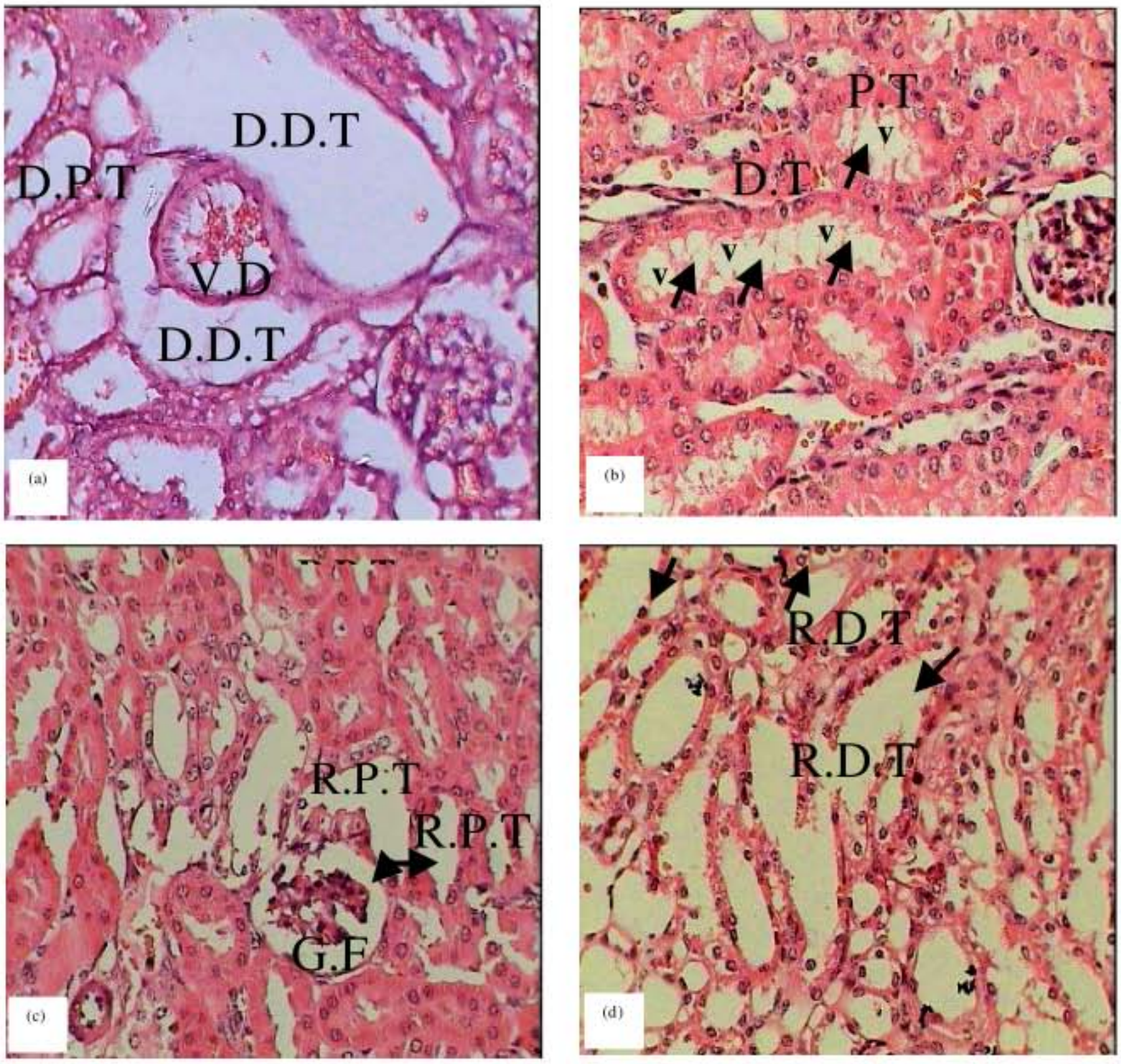

Fig. 6: (a) Kidney cross section (c.s.) of animal treated with 30 mg kg^{-1} dose for 6 weeks (group GIII), illustrates abnormal dilatation and irregular shapes of both the distal (D.D.T.) and proximal tubules (D.P.T.), also notice a vasodilatation (VD) of a blood vessel in the center. (x400, H and E stains). (b) Kidney (c.s.) of treated animal of group (GIII), observes the accumulation of the empty vacuoles (v) (arrows) inside the lumens of the distal tubule (D.T.) and proximal tubule (P.T.) (x400, H anmd E stain). (c) Kidney (c.s.) of treated animal of group (GIII), shows severe rupture of the proximal tubule walls (P.T.R.) (arrow) accompanied with severe fragmentation and destruction of the glomerulus (G.F.). (x400). (d) Kidney (c.s.) of treated animal of the same group, observes the ruptures of the distal tubules walls (D.T.R.) (arrows). (x400, H and E stains)

reported marked histological changes in the mice kidneys resulted from the treatment with anabolic drugs, these abnormal histological changes appeared in the form of abnormal dilatations of the proximal and distal convoluted tubules. On the other hand, in regard the mechanism of action, which may explain how Sustanon doses in particular can produce these observed nephritic histological damages, it is unfortunately still unknown. In spit of that there are a few available studies related to other types of the anabolic androgenic drugs provided some hypotheses about the mechanism. For instance, Welder *et al.* (1995) study suggested that the toxic effects induced by abusing these anabolic drugs for long period on the target organs such as liver and kidney occurred through the accumulation of certain toxic metabolites of testosterone such a (17α-19-nortestosterone and 17α-testosterone). Furthermore, the study of Wu and Eckerdstein (1997) reported that some types of anabolic steroid are able to induce massive necrosis and damages in the target organs in the form of chromatin

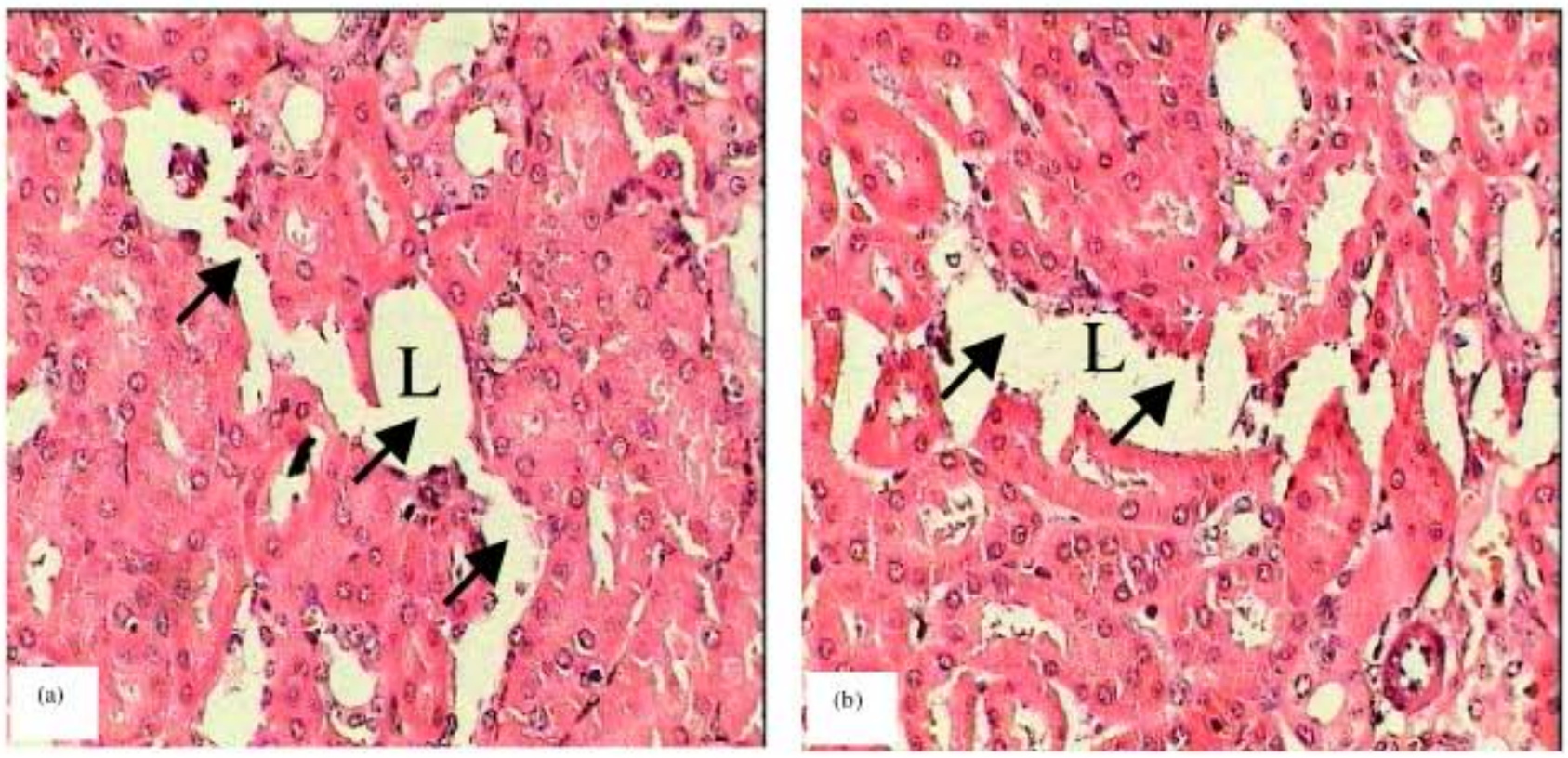

Fig. 7: (a-b) Two light micrographs of kidney (c.s.) of animals treated with 30 mg kg^{-1} dose for 6 weeks (group GIII), show wide destructions of the normal histological structure of the kidney in the form of severe lacerations (L) (arrows) inside the nephritic tissues. (x400, H and E stains)

condensation, DNA strand breakage and cytoplasmic shrinkage. Other investigators such as Draisci *et al.* (2000) and Zaugg *et al.* (2001) believed that abusing anabolic androgenic drugs cause cellular damages in the target organs such as the kidneys by damaging the DNA structure. Moreover, Behrendt and Boffin (2004) believed that abusing anabolic androgenic drugs produce multiple cellular toxic effects by inducing mitochondrial damages. The study showed mitochondria swollen and elongated accompanied with cristae destruction due to the effects of these drugs, these mitochondrial damages will definitely lead to cellular death because of the role of the mitochondria in supplying the cells with energy. It can be concluded from the present histopatholgical results that abusing Sustanon for long periods by athletes can induce serious histological damages in the kidneys which may lead to severe renal complications such as failure in late stages. Another important point which can be concluded from this study, is that physicians should take the renal disorders in mind seriously as a predictable and potential complications resulting from abusing these drugs such as Sustanon. Finally, the present study suggests and recommends that athletes and youths should be supplied with much more medical enlightenment about the health risks and the complications which resulted from abusing these drugs through media. At the same time, the official and medical control and restrictions on these drugs should be increased to prevent the abusers from obtaining these drugs.

REFERENCES

Al-Tayib, Y.A., 2004. The effect of melatonin on molybdenum hydroxylases activities of kidney and small intestine of guinea pigs. J. Egypt. Germ. Soci. Zool., 43A: 203-213.

Behrendt, H. and H. Boffin, 2004. Myocardial cell lesions caused by an anabolic drugs abuse. Cell Tissue Res., 181: 423-426.

Beotra, A., 2005. Drug Abuse in Sport. Control Center of Sports Authority of India, New Delhi, India.

Culling, C.F.A., 1974. Hand Book of Histopathological and Histochemical Techniques. 3rd Edn., Trowbridge and Esher, New York.

Draisci, R., L. Palleschi, E. Ferretti and P. Cammarata, 2000. Quantitation of anabolic Hormones and their metabolites in bovine Serum and urine by liquid chromatography Trandem mass spectrometry. J. Chematogap. Analysis., 99: 1293-1293.

Fineschi, V., I. Riezzo, F. Centini, E. Silingardi, M. Licata, G. Beduschi and S.B. Karch, 2007. Sudden cardiac death during anabolic steroid abuse: Morphologic and toxicologic findings in two fatal cases of bodybuilders. Int. J. Legal Med., 121: 48-53.

Fitch, K.D., 2008. Androgenic-anabolic steroids and the Olympic games. Asian J. Androl., 10: 384-390.

Habscheid, W., U. Abele and H.H. Dahm, 1999. Severe cholestasis with kidney failure from Anabolic steroids in bodybuilder. J. Dtsch. Med. Wochenschr, 124: 1029-1029.

Hartgens, F. and H. Kuipers, 2004. Effects of Androgenic-anabolic steroids in athletes. J. Sport Med., 34: 513-522.

Hartung , R., J. Gerth, R. Fünfstück and G. Stein, 2001. End-stage renal disease in a bodybuilder: A multifactorial process or simply doping?. J. Nephrol. Dial. Transplant., 16: 163-165.

Harvey, R.A. and P.C. Champe, 2002. The Lippincotts Illustrated Reviews of Pharmacology. 2nd Edn., JB Lippincott Co., New York, USA..

Hausmann, R., S. Hammer and P. Betz, 1998. Performance enhancing drugs (doping agents) and sudden death: A case report and review of the literature. Int. J. Legal Med., 111: 261-264.

Hoseini, L., J. Roozbeb, M. Saqheb and A. Noorafshan, 2009. Nandrolone decanoate increases the volume but not the length of the proximal and distal convoluted tubules of mouse kidney. Micron. J., 40: 226-230.

Johansson, S.P., F.G. Nyberg and L. Chahl, 2002. The anabolic androgenic steroid, nandrolone decanoate, increase the density of fos-like immunoreactive neurons in limbic regions of guinea pigs brain. Eurp. J. Neurosci., 15: 539-544.

Karch, S.B., 1997. Drugs Abuse Hand Book. 3th Edn., CRC Press, London, UK., ISBN-10: 0849316901.

Karila, T., 2003. Adverse Effects of Anabolic Androgenic Steroids on the Cardiovascular, Metabolic and Reproductive Systems of Anabolic Substance Abusers. University of Helsinki Press, Helsinki.

Kennedy, M.C. and C.F. Lawrence, 1993. Anabolic steroid abuse and cardiac death. Med. J. Australian, 158: 346-346.

Kindermann, W., 2006. Cardiovascular side effects of anabolic-androgenic steroids. J. Herz., 31: 566-573.

Lenehan, P., 2003. Anabolic Steroids. 2nd Edn., Taylor and Francis Inc., New York, USA., ISBN-10: 0415280303.

Modlinski, R. and K. Fields, 2006. The effect of Anabolic steroids on gastrointestinal system, Kidneys and adrenal glands. J. Curr. Sport Med. Rep., 5: 104-109.

Monaghan, L., 2001. Bodybuiling, Drugs and Risk. 1st Edn., Taylor and Francis Inc., New York, USA., ISBN-10: 041522683X.

Ryan, C. and L. Richard, 2005. Abuse of supraphysiologic doses of anabolic steroids. Southern Med. J., 98: 555-555.

Segura, J., S. Pichini, S. Peng and D. Torre, 2000. Hair analysis and delectability of single dose Administration of androgenic steroid ester. J. Forensic Sci. Int., 107: 347-59.

Socas, L., M. Zumbado, A. Romos, J. Hernadez and L. Boada, 2005. Hepatocellular adenomas associated with anabolic androgenic steroid abuse in body builders: A report of two cases and a review of the literature. Br. J. Sport Med., 39: 27-41.

Stimac, D., S. Miliæ, R.D. Dintinjana, D. Kovac and S. Ristiæ, 2002. Androgenic anabolic steroids induced toxic hepatitis. J. Clin. Gastrointerol., 35: 350-352.

Tahtamouni, L., N. Mustafa, A. Al-Muthana, I. Hassan, M. Abdalla and S. Yasin, 2008. Prevalence and risk factors for anabolic androgenic steroid abuse among Jordanian collegiate students and athletes. Eurp. J. Pub. Health, 28: 661-665.

Urhausen, A., T. Albers and W. Tindermann, 2004. Are the cardiac effects of anabolic steroid abuse in strength athletes reversible?. Heart J., 90: 496-501.

Welder, A., J. Robertson and R. Melchert, 1995. Toxic effects of anabolic-androgenic Steroids in primary rat hepatic cell culture. J. Pharmacol. Toxicol. Methods., 33: 187-195.

Wills, S., 2005. Drugs of Abuse. 2nd Edn., Pharmaceutical Press, London, UK., ISBN-10: 0853695822.

Wu, F. and A.V. Eckardstein, 1997. Androgens and coronary artery disease. Endocrinol. Rev., 24: 183-217.

Yesalis, C.E., 2000. Anabolic Steroids in Sport and Exercise. Human Kinetics, New York, USA., ISBN-10: 0880117869.

Zaugg, M., N. Jamali, E. Lucchinerri, S. Shafiq and M. Siddiqi, 2001. Anabolic androgenic steroids induce apoptotic cell death in adult rat ventricular myocytes. J. Cellular Physiol., 187: 90-95.

Zeier, M., R. Schönherr, K. Amann and E. Ritz, 1998. Effects of testosterone on glomerular growth after uninephrectomy. Nephrol Dial. Transplant., 13: 2234-2240.