**Health Science Monitor**
2025; 4(1): 29-36
Published online (http://hsm.umsu.ac.ir)

Original Article

# Microscopic alterations in the hepatic architecture of male albino rats following administration of nandrolone decanoate

**Parvaiz Ahmad Lone [1], Bashir Ahmad Shah [2], Nazish Aslam [3], Mudasir Ahmad Khan [4*]**

[1] *Senior Resident, Department of Anatomy, Government Medical College, Anantnag, India*
[2] *Professor, Postgraduate Department of Anatomy, Government Medical College, Srinagar, India*
[3] *Senior Resident, Department of Anatomy, Government Medical College, Srinagar, India*
[4] *Assistant Professor, Department of Anatomy, Government Medical College, Anantnag, India*

***Corresponding author:** Mudasir Ahmad Khan, **Address**: Department of Anatomy, Government Medical College, Anantnag, **Email**: drmudasirkhan73@gmail.com, **Tel**: +917006107520

## Abstract

***Background & Aims*:** The synthetic testosterone analog nandrolone decanoate (ND) is one of the most commonly used anabolic androgenic steroids (AAS) among athletes and teens. Athletes who consume anabolic androgenic steroids regularly are more likely to develop liver issues, although the exact process is unknown. This experimental investigation aims to evaluate the impact of nandrolone decanoate treatment on the hepatic architecture of male rats.

***Materials & Methods*:** For the purpose of this study, twenty male albino rats were separated into two groups. Group A received peanut oil as a control, whereas Group B received weekly injections of nandrolone decanoate at a dose of 10 mg/kg body weight for eight weeks. The rats were sacrificed after 8 weeks, following the guidelines provided by the Ethics Committee. After the rats were dissected, the liver tissue was collected and fixed in accordance with standard histological protocols. Hematoxylin and eosin were used to stain sections, and microscopic observations were recorded in both groups.

***Results*:** After 8 weeks, microscopic examination of the liver in the control group revealed no noticeable changes, while the group treated with nandrolone decanoate displayed large Kupffer cells, vacuolation of the hepatocytes, congestion of the central vein, and dilatation of the hepatic sinusoids.

***Conclusion*:** The research showed that abusing nandrolone decanoate causes liver issues such as hepatic sinusoidal dilatation, congestion, and vacuolation of hepatocytes. It also causes congestion in the central vein. This research highlights the need for well-designed trials with appropriate dosage considerations, as well as the examination of the long-term effects of nandrolone decanoate.

***Keywords*:** Anabolic androgenic steroids, Liver histopathology, Nandrolone decanoate

**Received 02 September 2024; accepted for publication 07 December 2024**

## Introduction

Anabolic androgenic steroids (AAS) were developed in an effort to create a steroid with potent anabolic effects that would resemble testosterone (1). AAS were prohibited in many organized sports, but because of their anabolic properties, they gained a lot of popularity among professional and recreational athletes (2, 3). To enhance their athletic performance muscular mass, and strength weightlifters, bodybuilders, swimmers, and cyclists are the athletes who most frequently utilize these components (4, 5). Unfortunately, these people may consume doses that are up to 100 times higher than those recommended for therapeutic purposes, which has detrimental consequences on numerous organ systems (6).

Anabolic androgenic steroids are effective in helping treat a wide range of illnesses, including anemia, osteoporosis, testosterone replacement therapy, muscle atrophy-causing disorders, cachexia driven by some malignancies, and HIV. In adult males, long-term hypogonadism is linked to impaired bone production. There is not a single AAS preparation that works better than the others when treating muscle-wasting diseases (7). Although AAS has been explored as replacement treatment for male andropause, further research is needed before it can be widely utilized to improve the quality of life for aging men (8). Nandrolone is derived from 19-nortestosterone and is often administrated as depot preparations.

Among athletes, it is currently one of the most popular AAS (9). Although its anabolic effects are greater than those of testosterone, prolonged use can lead to serious adverse consequences, including changes in the structure and function of the liver and potentially the development of hepatocellular adenoma (10). Long-term, uncontrolled use of nandrolone can result in negative effects such as liver toxicity, thyroid dysfunction and cardiovascular toxicities, despites its therapeutic benefits (11).

Adverse effects are dependent on dosage, dose interval, and individual sensitivity (12). Abnormal liver function, (13) jaundice-associated peliosis, hepatitis, increased or decreased libido, (14) inhibition of spermatogenesis, testicular atrophy, gynecomastia, hypertension and epididymitis, bladder irritability, reduced urine flow (15, 16) benign prostate hypertrophy and priapism have been documented (17, 18). The rising incidence of AAS use among high school students has resulted in a major increase in misuse. While adverse effects on liver function have been recorded, the study seeks to bridge a knowledge vacuum by evaluating the impact of AAS on liver tissue, giving important data to healthcare professionals and academics.

The study's originality stems from its focus on the specific impact of anabolic androgenic steroids (AAS) on liver tissue, which has not been fully investigated in the current literature. The project intends to fill a major information gap by investigating the precise pathological and physiological effects of AAS, particularly in terms of recreational and non-medical use, and to advise doctors, healthcare providers, and policymakers. Furthermore, it targets the increased prevalence of AAS usage among younger groups, with the goal of providing targeted insights that can lead to better health outcomes and educational programs about the harms of steroid use.

## Materials & Methods

For the purpose of the study, nandrolone decanoate injection was acquired from the market. Wistar Albino rats served as the experimental animals. The Central Animal House of the Medical College provided the rats for the experiment. The Animal Institutional Ethics Committee, which was established specifically for this purpose, provided the necessary approval for the use of animals under code number MC-421 (GMCS-2020).

### Experimental Design

Twenty male albino rats were divided into two groups. Group A: Five rats, which acted as the control group received a 90% peanut oil injection. Group B: Fifteen rats received injectable nandrolone decanoate at a dose of 10 mg/kg body weight per week for 8 weeks. (Dosage calculation: 10 mg/kg body weight, concentration: 25 mg/ml, rat weight: 200 grams. Therefore, one dose is equivalent to 0.08 milliliters.)

The Committee for the Purpose of Control and Supervision of Experiment on Animals states that maintaining a control group of this size is sufficient. After the eighth week, the animals were sacrificed and dissected following the guidelines established by the "Committee for the Purpose of Control and Supervision of Experiments on Animals". Anesthesia for the animals, was administered using inhalation of chloroform. In the Animal House of GMC Srinagar, rats were dissected under meticulously controlled conditions with the assistance of distinguished personnel. The following materials were used: 70% ethanol as a disinfectant, 10% neutral buffered formalin as a preservative, and normal saline for rinsing. The rats were thoroughly examined, and information on their weight, activity level, skin health, and the presence of any external parasites was recorded. Every orifice was checked for leaks, and any visible lesions on the body's exterior were appropriately noted. The sacrificed rat was stretched out and pinned at the fore and hind feet while lying supine on the dissection tray. A swab of 70% ethanol was used over the entire ventral surface, extending from the nose to the anus, to sterilize and eliminate hair and dust. A midline incision was made from the point of the lower jaw to the pubic region by pinching up the skin in the mid-ventral line and keeping the bottom blade of the scissors horizontal to avoid damaging the body wall underneath. Pinching the body wall muscles, from the pubic symphysis to the lower edge of the sternum allowed entry into the abdominal cavity. The lower ribs, which define the thoracic line, were used as a reference to cut the abdomen wall. This approach resulted in less bleeding, making the midline incision preferable. Without causing any damage to the structures, the abdominal wall was pulled aside, and the organs were examined. The thoracic cage, which included the ribs and sternum, was visible from above. Other features included the white xiphoid cartilage, three liver lobes, the small and large intestines, the rectum, and the testes.

**Histological Techniques**

The liver specimen was processed using standard histological techniques, starting with fixation in a 10% formalin solution for seven days, which preserved tissue structure. Following fixation, the specimen was dehydrated through a series of ethyl alcohol solutions and then cleared with xylene. It was then impregnated with molten paraffin wax at 58°C, embedded in molds, and allowed to solidify. Thin sections (6-8 microns) were cut with a microtome, floated in a water bath for smoothness, and mounted on labeled slides coated with Meyer's egg albumin solution. After drying, the slides were stained with Hematoxylin and Eosin for microscopic examination, and observations were recorded and photographed at magnifications of 10X and 20X.

## Results

On general examination, the animals were apparently healthy, alert, and feeding well, with, no hair loss, however; size and total body weight had increased (Prior to the research, all albino rats weighed 200 g and had a liver weight of 4 g). After the trial, the body weight of albino rats was 290-300 g, and the liver weight was 7 g.

**Group A**

Microscopic features: On microscopic examination the basic architecture of the liver was found to be preserved. No significant histological changes were observed in the rats.

**Group B**

Microscopic Features: The histopathological examination revealed congestion of hepatic sinusoids (Figure 1), dilatation of hepatic sinusoids (Figure 2), congestion of the central vein (Figure 3), large Kupffer cells (Figure 4), and vacuolation of hepatocytes, as shown in (Figure 5).

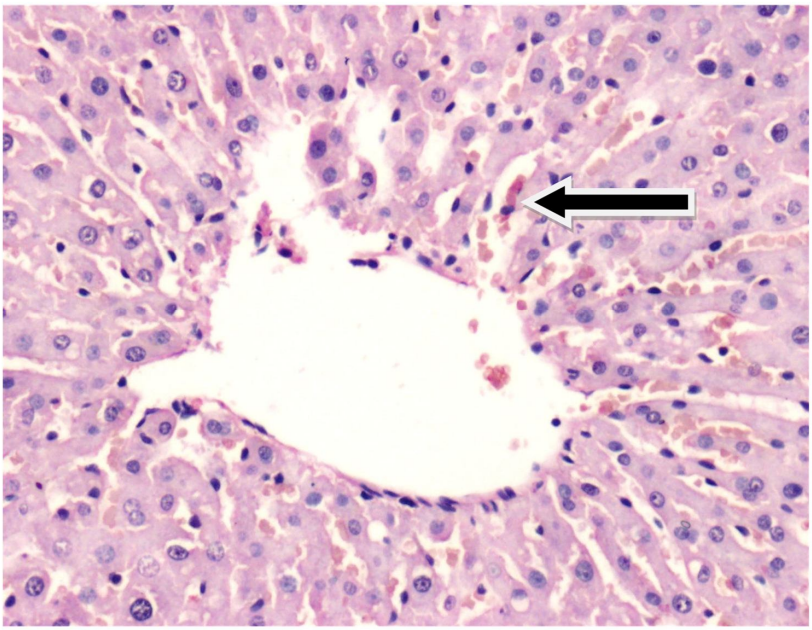

**Fig. 1.** Showing dilatation and congestion of hepatic sinusoids (black arrow) Stain: H & E, Magnification: 20x

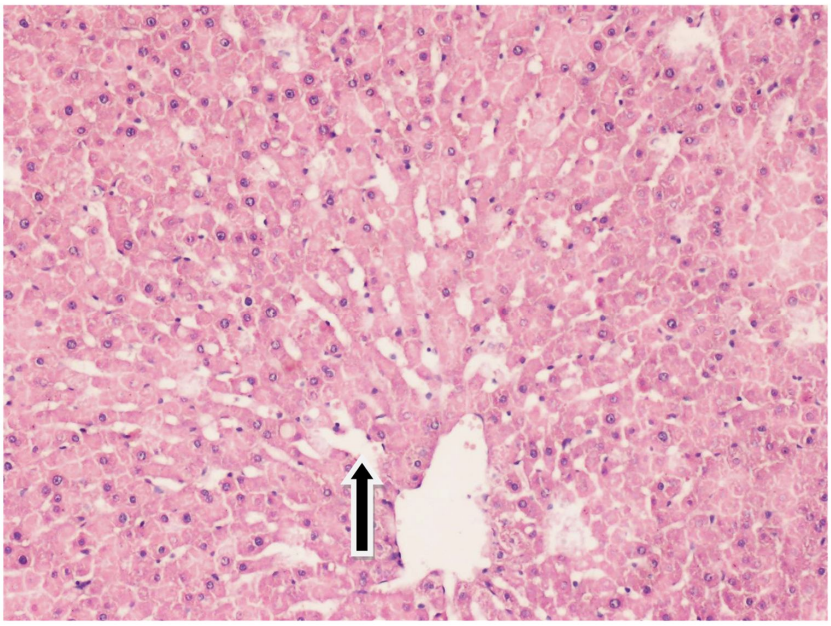

**Fig. 2.** Occasional dilatation of sinusoids (black arrow). Stain: H & E, Magnification: 20x

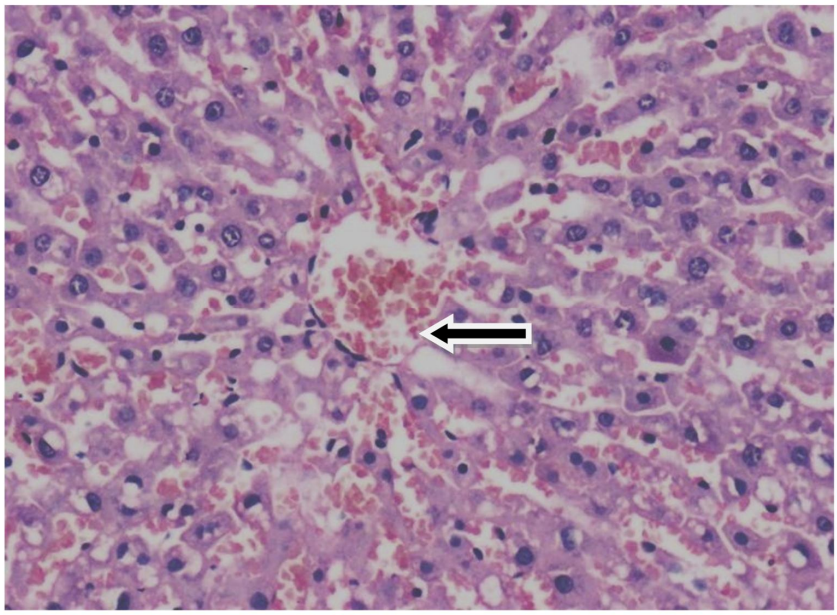

**Fig. 3.** Congested central vein (black arrow) with congestion and dilatation of hepatic sinusoids. Stain: H & E, Magnification: 20x

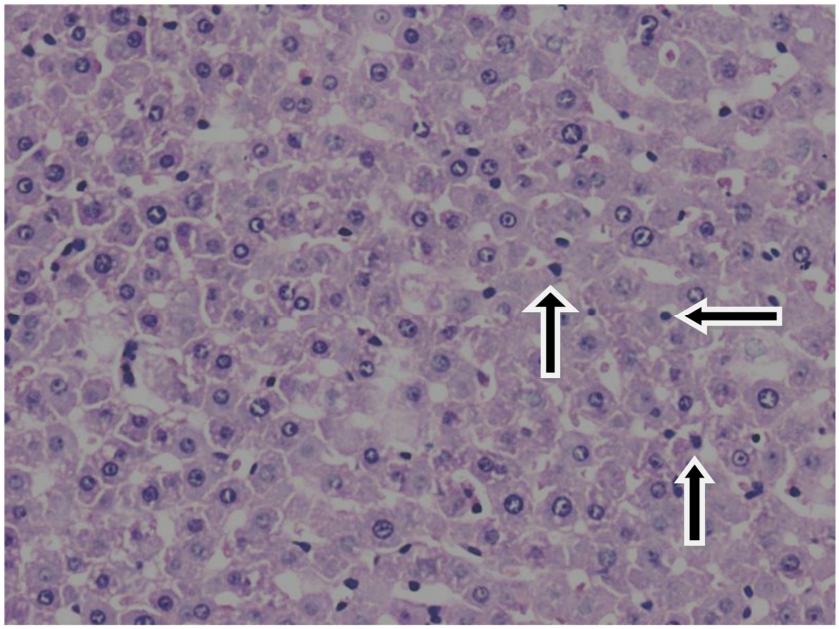

**Fig. 4.** Large Kupffer cells (black arrows) Stain: H & E, Magnification: 20x

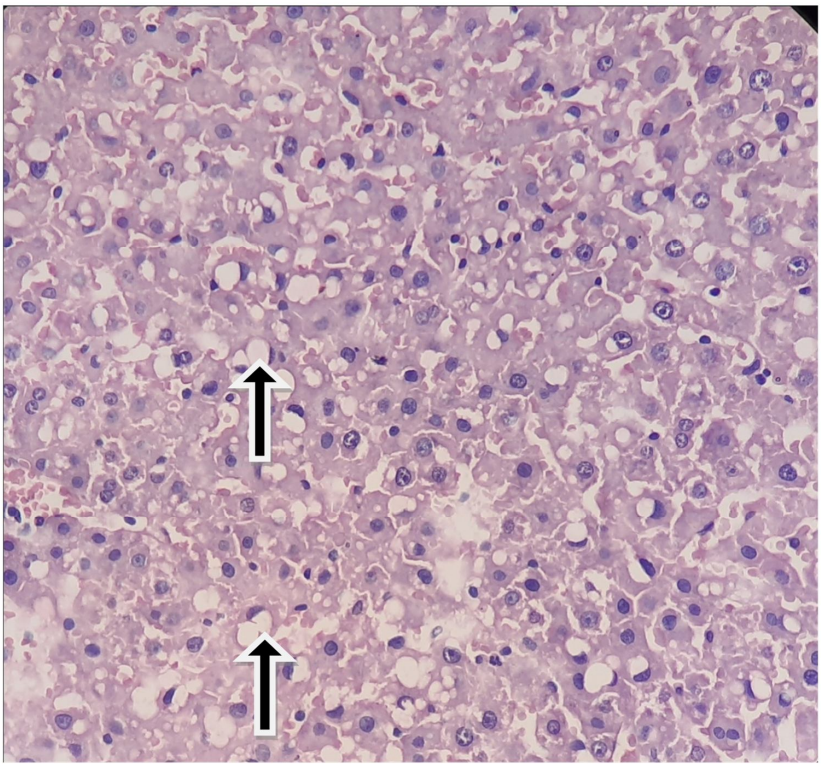

**Fig. 5.** Vacuolation of hepatocytes (black arrows). Stain: H & E, Magnification: 20x

## Discussion

The livers of two groups were investigated in this study. Group B's liver displayed symptoms of hepatocyte vacuolation, large Kupffer cells, central venous congestion, and hepatic sinusoidal dilatation. These findings supported the study's conclusion that nandrolone decanoate had an impact on rat liver function. Nandrolone decanoate causes histological changes in the liver due to a complex interplay of interrelated pathways that contribute to liver damage. Oxidative stress is a significant factor, in which an excess of reactive oxygen species overwhelms the liver's antioxidant defenses, leading to cellular damage, inflammation, and hepatocyte injury. The steroid also alters liver structure, causing hepatocyte expansion and lobular disintegration. This injury triggers inflammation and stimulates hepatic stellate cells, resulting in increased collagen deposition and fibrosis. Nandrolone affects lipid metabolism, causing fat buildup in hepatocytes (19). Changes such as hepatic sinusoidal dilatation and central venous congestion are associated with altered blood flow. Overall, the interaction of oxidative stress, inflammation, and metabolic disturbance reveals nandrolone decanoate's hepatotoxicity. Long-term injection of nandrolone decanoate caused considerable alterations in rats' liver tissue, lipid droplet accumulation (20). Similar histological alterations in rat liver tissue following nandrolone decanoate injection, including sinusoidal dilatation, and localized necrosis (21). The study discovered that nandrolone decanoate elevated serum liver enzymes, indicating probable liver injury.

The effects of nandrolone decanoate on the liver and kidneys of rats and discovered that the steroid caused

significant histological alterations in both organs (22). The study emphasizes the need for monitoring the liver and kidneys when using anabolic-androgenic steroids such as nandrolone decanoate. Nandrolone decanoate induced hepatotoxicity in rats, as evidenced by elevated liver enzymes, histological abnormalities, and oxidative stress (23). According to the study, nandrolone decanoate may cause liver damage through oxidative stress and inflammation (24). Effects of nandrolone decanoate on rat liver tissue showed that the steroid significantly altered the morphology of the liver, notably the size and shape of liver cells. The study emphasizes how scanning electron microscopy may be used to observe the effects of anabolic-androgenic steroids on liver tissue.

## Conclusion

According to this study, using nandrolone can cause hepatic abnormalities such as congestion of hepatic sinusoids, dilatation of hepatic sinusoids, congestion of the central vein, large Kupffer cells, and vacuolation of hepatocytes. As the main limitation of the current study was the low study population, the findings highlight and recommend the importance of future research into the long-term effects of these medications and the effects of toxic doses of nandrolone, as well as careful consideration of study design and dose.

## Acknowledgments

The faculty and all the academics whose works are referenced and cited are greatly appreciated.

## Author's Contributions

Parvaiz Ahmad Lone and Bashir Ahmad Shah conceptualization/study design, Nazish Aslam review, and Mudasir Ahmad Khan ethical oversight and correspondence.

## Data Availability

Upon reasonable request, the authors will provide the raw data that comprised the article's conclusions.

## Conflict of Interest

Authors declare there is no conflict of interest.

## Ethical Statement

This study was carried out following the Animal Institutional Ethical Committee's essential approval for the use of animals established for this purpose. MC-421 code number (GMCS-2020).

## Funding/Support

None declared.

## References

1. Angell P, Chester N, Green D, Somauroo J, Whyte G, George K. Anabolic steroids and cardiovascular risk. Sports Medicine. 42(2):119-34. doi: 10.2165/11598060-000000000-00000. PMID: 22229259.
2. Nieschlag E, Vorona E. Doping with anabolic androgenic steroids (AAS): Adverse effects on non-reproductive organs and functions. Reviews in Endocrine and Metabolic Disorders. 2015;16(3):199–211. doi: 10.1007/s11154-015-9320-5.
3. Piacentino D, Kotzalidis GD, Del Casale A, Aromatario MR, Pomara C, Girardi P, Sani G. Anabolic-androgenic steroid use and psychopathology in athletes. A systematic review. Current Neuropharmacology. 2015;13(1):101–21. doi: 10.2174/1570159X13666141210222725.
4. De Piccoli B, Giada F, Benettin A, Sartori F, Piccolo E. Anabolic steroid use in body builders: an echocardiographic study of left ventricle morphology and function. International Journal of Sports Medicine. 1991;12(4):408-12. doi: 10.1055/s-2007-1024703.
5. Rocha FL, Carmo EC, Roque FR, Krieger JE, Oliveira EM. et al. Anabolic steroids induce cardiac renin-angiotensin system and impair the beneficial effects of aerobic training in rats. American Journal of Physiology-Heart and Circulatory Physiology. 2007;293(6):H3575-83. doi: 10.1152/ajpheart.01251.2006.
6. Yesalis CE, Bahrke MS. Anabolic-androgenic steroids. Current issues. Sports Medicine. 1995;19(5):326-40. doi: 10.2165/00007256-199519050-00003.
7. Strawford A, Barbieri T, King J, Hellerstein MK. et al. Resistance exercise and supraphysiologic androgen therapy in eugonadal men with HIV-related weight loss: a randomized controlled trial. The Journal of The

American Medical Association. 1999;281(14):1282-90. doi: 10.1001/jama.281.14.1282.

8. Pärssinen M, Seppälä T. Steroid use and long-term health risks in former athletes. Sports Med. 2002;32(2):83-94. doi: 10.2165/00007256-200232020-00001.
9. Shahidi NT. A review of the chemistry, biological action, and clinical applications of anabolic-androgenic steroids. Clinical Therapeutics. 2001;23(9):1355-90. doi: 10.1016/s0149-2918(01)80114-4.
10. Frankenfeld SP, de Oliveira LP, Carvalho DP, Fortunato RS. et al. Nandrolone decanoate inhibits gluconeogenesis and decreases fasting glucose in Wistar male rats. The Journal of endocrinology. 2014;220(2):143-53. doi: 10.1530/JOE-13-0259.
11. Fortunato RS, Marassi MP, Chaves EA, Nascimento JH, Rosenthal D, Carvalho DP. Chronic administration of anabolic androgenic steroid alters murine thyroid function. Medicine & Science in Sports & Exercise. 2006;38(2):256-61. doi: 10.1249/01.mss.0000183357.19743.51.
12. Shabir, Naveera & Malik, Husna & Sajjad, Sumera & Nadeem Abbas, Muhammad. (2015). Effect of Nandrolone Decanoate, Boldenone Undecylenate on Renal Status of Rabbits (Oryctolagus cuniculus). 14. 432-438. 10.5829/idosi.gv.2015.14.03.92201.
13. Bento-Silva MT, Martins M do C de C e, Torres-Leal FL, Barros TL, Carvalho IL do NF de, Carvalho Filho HA, et al. 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. Brazilian Journal of Pharmaceutical Sciences. 2010;46(1):79–89. Available from: https://doi.org/10.1590/S1984-82502010000100009
14. Shahidi NT. A review of the chemistry, biological action, and clinical applications of anabolic-androgenic steroids. Clinical Therapeutics. 2001;23(9):1355-90. doi: 10.1016/s0149-2918(01)80114-4.
15. M, Neri M, Riezzo I, Fineschi V. Side effects of AAS abuse: an overview. Mini-Reviews in Medicinal Chemistry. 2011;11(5):374-89. doi: 10.2174/138955711795445925
16. van Amsterdam J, Opperhuizen A, Hartgens F. Adverse health effects of anabolic-androgenic steroids. Regulatory Toxicology and Pharmacology. 2010;57(1):117-23. doi: 10.1016/j.yrtph.2010.02.001.
17. Brower KJ. Anabolic steroid abuse and dependence. Current Psychiatry Reports. 2002;4(5):377-87. doi: 10.1007/s11920-002-0086-6.
18. Basaria S. Androgen abuse in athletes: detection and consequences. The Journal of Clinical Endocrinology & Metabolism. 2010;95(4):1533-43. doi: 10.1210/jc.2009-1579.
19. Samieinasab MR, Shahraki MR, Samieinasab F, Najafi S. Influence of nandrolone decanoate administration on serum lipids and liver enzymes in rats. ARYA Atheroscler. 2015;11(4):256-60.
20. Ghorbanihaghjo A, Argani H, Rohbaninoubar M, Rashtchizadeh N. Effect of Nandrolone Decanoate on serum lipoprotein (a) and its isoforms in hemodialysis patients. Lipids in Health and Disease 2004; 3: 16.
21. Hartgens F, Rietjens G, Keizer HA, Kuipers H, Wolffenbuttel BH. Effects of androgenic-anabolic steroids on apolipoproteins and lipoprotein (a). British Journal of Sports Medicine. 2004; 38(3): 253-9
22. Petrovic A, Vukadin S, Sikora R, Bojanic K, Smolic R, Plavec D, Wu GY, Smolic M. Anabolic androgenic steroid-induced liver injury: An update. World Journal of Gastroenterology. 2022;28(26):3071-3080. doi: 10.3748/wjg.v28.i26.3071.
23. Filho P, Gomes S, Forte P, Lima GA, Júnior S, Meneses G, et al. Kidney disease associated with androgenic-anabolic steroids and vitamin supplements abuse: Be aware! Nefrologia (Engl Ed). 2020;40(1):26-31. English, Spanish. doi: 10.1016/j.nefro.2019.06.003.
24. Vieira, Rodolfo Paula1; França, Rafaela Ferreira2; Damaceno-Rodrigues, Nilsa Regina1; Dolhnikoff, Marisa1; Caldini, Élia Garcia1; Carvalho, Celso Ricardo Fernandes3; Ribeiro, Welington2. Dose-Dependent Hepatic Response to Subchronic Administration of Nandrolone Decanoate. Medicine & Science in Sports & Exercise. 40(5):p 842-847, 2008. DOI: 10.1249/MSS.0b013e3181666f1c