



Nandrolone Decanoate; Overview and Effects on Body systems

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Abstract

Background: Nandrolone decanoate, is an androgen and anabolic steroid (AAS) medication sold under the brand name Deca-Durabolin. It is used largely in the treatment of anemias and wasting syndromes, as well as osteoporosis in menopausal women. It is administrated by injection into muscle or fat once every one to four weeks. Compared to testosterone propionate, nandrolone decanoate is considered to have strong anabolic effects but weak androgenic effects. In particular, nandrolone esters are thought to have the highest ratio of anabolic to androgenic effects of any AAS. The low androgenicity of nandrolone decanoate is thought to be due to the fact that nandrolone is inactivated by 5α -reductase via transformation into the low-affinity androgen receptor (AR) ligand 5α -dihydranandrolone. This is thought to result in a lower incidence and magnitude of side effects. Nandrolone decanoate is a prodrug of nandrolone. it is an androgen and anabolic steroid with enhanced anabolic effects and reduced androgenic effects unlike testosterone. The side effects of nandrolone decanoate are related to dose, individual sensitivity and interval of treatment. The most common side effect of nandrolone decanoate is virilization (masculinization) in women.

Keywords: Nandrolone Decanoate

Introduction

Nandrolone decanoate, is an androgen and anabolic steroid (AAS) medication sold under the brand name Deca-Durabolin. It is used largely in the treatment of anemias and wasting syndromes, as well as osteoporosis in menopausal women. It is administrated by injection into muscle or fat once every one to four weeks (1).

In 1960 nandrolone decanoate was first described as the second nandrolone ester following nandrolone phenylpropionate (NPP). Then it was used medically in 1962. It is also one of the most broadly used AAS worldwide. In addition to its medical use, nandrolone decanoate is the most widely used AAS for purposes of improving physique and performance. The drug is a controlled substance in many countries and so non-medical use is generally illegal (1).

Nandrolone is encompassed in the group of class II AASs, which is composed of 19-nortestosterone-derivates. In general, AASs is a rapidly growing group of synthetic androgens used both clinically and illegitimately(2).

Compared to testosterone propionate, nandrolone decanoate is considered to have strong anabolic effects but weak androgenic effects. In particular, nandrolone esters are thought to have the highest ratio of anabolic to androgenic effects of any AAS. The low androgenicity of nandrolone decanoate is thought to be due to the fact that nandrolone is inactivated by 5α -reductase via transformation into the low-affinity androgen receptor (AR) ligand 5α -dihydranandrolone. This is thought to result in a lower incidence and magnitude of side effects (3).

Nandrolone has very low affinity for human serum sex hormone-binding globulin (SHBG), about 5% of that of testosterone and 1% of that of dihydrotestosterone (DHT). It is mainly metabolized by the enzyme 5α -reductase, into 5α -dihydronandrolone, 19-norandrosterone, and 19-noretiocholanolone, which can be detected in urine (4).

Nandrolone can be used clinically for burns, trauma, surgery, radiation therapy, and various forms of anemia. It has also been used for the treatment of chronic kidney disease, inoperable breast cancer, osteoporosis in postmenopausal women, for patients on long-term corticosteroid therapy, as well as a therapeutic aid in conditions characterized by a negative nitrogen balance. The drug is used also to preserve muscle mass in acquired immunodeficiency syndrome (AIDS) associated wasting syndrome (2).

The compound is famous not only among adults, but also adolescents because of its anabolic, muscle-building, properties (5). Skeletal muscle can be considered as the primary target tissue for the anabolic effects of AAS. These anabolic effects are mediated by androgenic receptors which, after exposure to AAS, are up-regulated and their number increases with bodybuilding. Therefore, AAS determine an increase in muscle size as a consequence of dose-dependent hypertrophy, resulting in an increase of the cross-sectional areas of both type I and type II muscle fibers and myonuclear domains. Moreover, it has been reported that AASs can increase tolerance to exercise by making the muscles more capable of resisting overload, thereby shielding them from muscle fiber damage and improving the level of protein synthesis during recovery. It is administered via intramuscular injection and is metabolized to 3-norandrosterone in a similar manner to testosterone, by 5α -reductase (6).

Acute side effects of Nandrolone decanoate include fluid retention, headaches, hypertension, gastrointestinal irritation, abdominal pain, diarrhea, jaundice and menstrual abnormalities. However chronic effects of AAS abuse, involve several neuropsychiatric and behavioral effects in addition to a wide range of somatic consequences, as it may exert negative effects on cardiovascular, hematological, endocrine, reproductive, renal, hepatic, musculoskeletal, immunologic and cerebrovascular systems (7).

Athletes in power sports such as weightlifting and bodybuilding use high doses of AASs to increase their muscle mass and improve their overall performance (8).

Non-athletes also abuse AASs. Nandrolone decanoate (ND) injection has been classified as a Schedule III controlled substance under the Anabolic Steroids Control Act of 1990. In addition, AASs are listed in the WADA (World Anti-Doping Agency) forbidden list due to its serious health risks. The nonmedical use of AASs is banned by most sports organizations. The abuse of these drugs has become a major health problem (9).

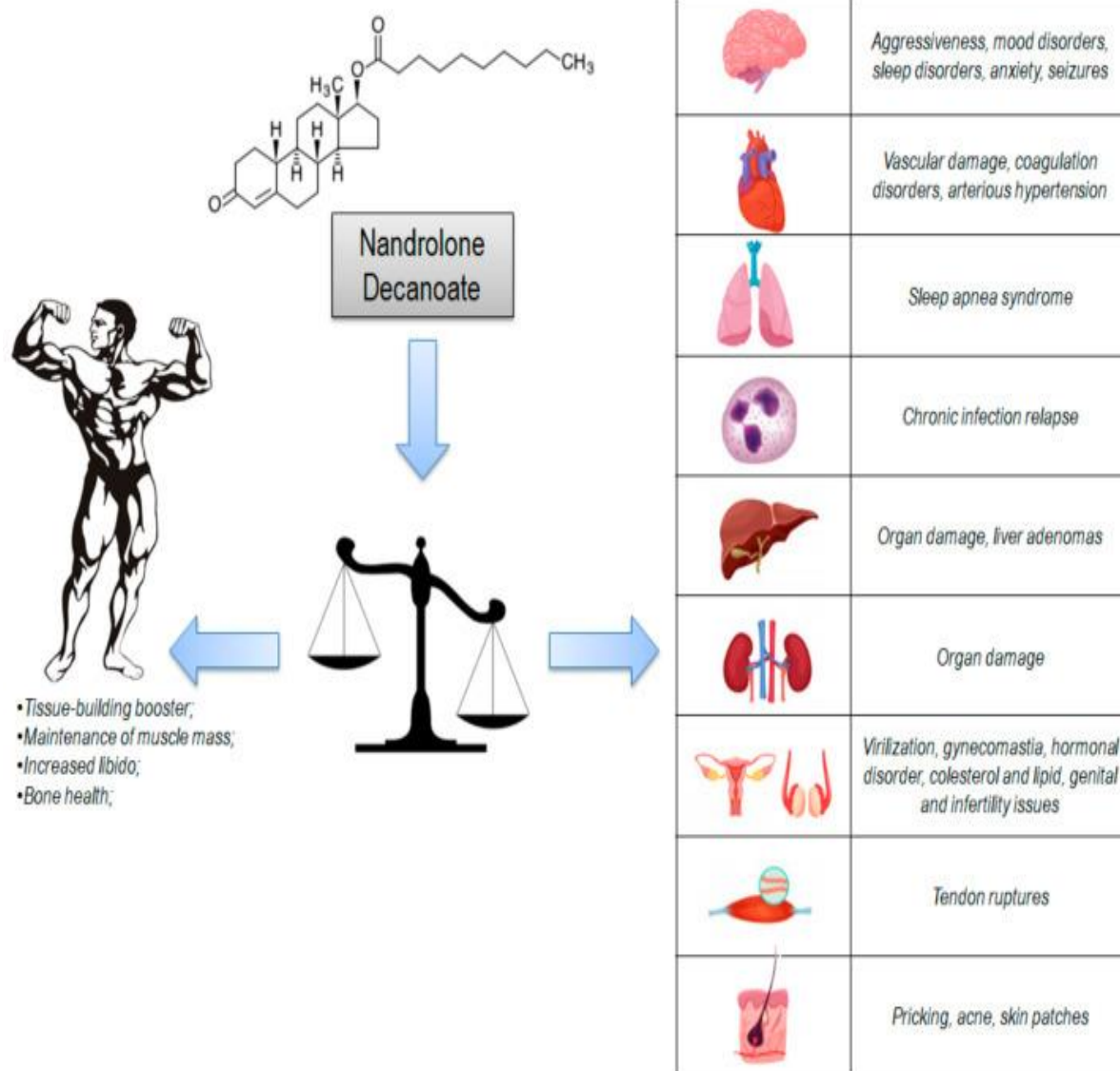


Fig. (1): There is a balance between known positive effects and underestimated or unknown side effects, because nandrolone decanoate is a molecule that affects several systems at the same time and sometimes in an irreversible way (2).

Pharmacology

Chemistry

Nandrolone decanoate, or nandrolone 17 β -decanoate, is a synthetic estrane steroid and a derivative of testosterone. It is an androgen ester; specifically, it is the C17 β decylate (decanoate) ester of nandrolone (19-nortestosterone), which itself is the 19-demethylated analogue of testosterone (10).

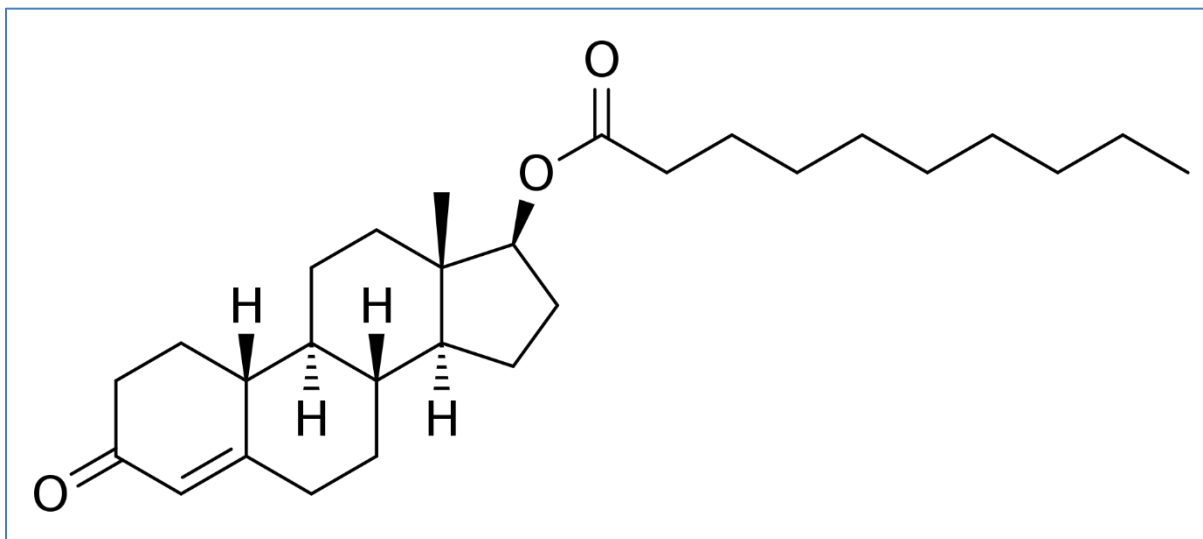


Fig. (2): Chemical structure of nandrolone decanoate (*II*).

Pharmacodynamics

Nandrolone decanoate is a prodrug of nandrolone. It is an androgen and anabolic steroid with enhanced anabolic effects and reduced androgenic effects unlike testosterone (*I*).

Potency ratios of the anabolic effects to androgenic effects are 3.29–4.92 and 0.31–0.41 (index value 10.6–12.1 or about an 11:1 ratio of myotrophic to androgenic effect) relative to testosterone propionate. This is defined specifically on the basis of a rodent model in which change in the weights of the rat bulbocavernosus/levator ani muscle ("anabolic" or "myotrophic" activity) and the rat ventral prostate or seminal vesicles ("androgenic" activity) are compared with testosterone and then used to form a ratio (*I2*).

The low androgenicity of nandrolone decanoate is thought to be due to the fact that nandrolone is inactivated by 5 α -reductase via transformation into the low-affinity AR ligand 5 α -dihydrondrolone in specific tissues including the skin, hair follicles, prostate gland, liver, and brain. Whereas, many other AAS like testosterone are potentiated via transformation by 5 α -reductase into more potent AR agonists like DHT in such tissues (*I*). This is thought to result in a much lower incidence and magnitude of facial/body hair growth, scalp hair loss, and possibly prostate issues like prostate enlargement and prostate cancer with nandrolone esters relative to testosterone. Moreover, nandrolone decanoate has low estrogenic activity (via its metabolite estradiol) and moderate progestogenic activity. This may result in side-effects such as fluid retention and gynecomastia. (*I*).

Pharmacokinetics

Nandrolone decanoate when intramuscularly injected results in the formation of a long-lasting depot in the muscle then become stored unchanged and slowly absorbed into the body (*I3*) (*Thomas, 2012*).

Once in the circulation, it is converted into nandrolone, which is the active form of the drug. There is a sharp spike in nandrolone levels 24 to 48 hours after injection of nandrolone decanoate, followed by a steady decline to baseline levels within approximately two or three weeks (*I*).

The bioavailability of nandrolone decanoate is 53 to 73% with intramuscular injection and differs with the site of injection. It was found that the highest bioavailability was seen when injected into the gluteal muscle. Nandrolone is present in both bound and free fractions in the blood. It is highly bound to protein. Like testosterone. It has very low affinity for sex hormone-binding globulin (SHBG), about 5% of that of testosterone and 1% of that of DHT (*I3*).

Rapid hydrolysis of nandrolone decanoate occurs in the blood by esterase enzyme into nandrolone, with a terminal half-life of one hour or less (*I3*). It does not appear to be hydrolyzed in muscle or fat (*I4*).

Metabolism of Nandrolone occurs in the liver and in a similar way to that of testosterone, including reduction by 5 α -reductase and 5 β -reductase, dehydrogenation by 3 α -hydroxysteroid dehydrogenase, 3 β -hydroxysteroid dehydrogenase, and 17 β -hydroxysteroid dehydrogenase, and conjugation. The metabolites of nandrolone include 5 α -dihydrondrolone, 19-norandrosterone, and 19-noretiocholanolone, with 19-

norandrosterone being the major metabolite. Other metabolites include 19-norandrostenedione, 19-norandrostane diols, 19-norepiandrosterone, and conjugates (**13**) Nandrolone also undergoes aromatization into estradiol similarly to testosterone, though at a rate of only about 20% of that of testosterone or possibly even less; one study found virtually no aromatization of nandrolone in men (**1**).

The elimination half-life of nandrolone decanoate administered by intramuscular injection is approximately 6 to 12 days. Some studies have found that a single 50 to 100 mg intramuscular injection had been eliminated in 18 to 25 days (**15**).

The blood half-life for the combined process of hydrolysis into nandrolone and elimination of nandrolone is 4.3 hours. Nandrolone and its metabolites are excreted in the urine, mainly in the form of conjugates (**13**).

Nandrolone decanoate subcutaneous injection appear to have a similar effect of nandrolone when administered by intramuscular injection. The pharmacokinetics of both subcutaneous and intramuscular nandrolone decanoate was the same. However, subcutaneous injection is considered to be more convenient, easier and less painful compared to intramuscular injection. In addition, research suggests that most intramuscular injections in practice are in fact subcutaneous injections (**16**).

Side Effects

The side effects of nandrolone decanoate are related to dose, individual sensitivity and interval of treatment. The most common side effect of nandrolone decanoate is virilization (masculinization) in women. Uncommon side effects of nandrolone decanoate at recommended dosages include fluid retention, testicular atrophy, inhibition of spermatogenesis, erectile dysfunction, gynecomastia, increased penis size in pre-pubertal boys, clitoral hypertrophy, increased pubic hair growth, oligomenorrhea, amenorrhea, hyperlipidemia, decreased HDL, increased hemoglobin (to abnormal high levels), hypertension, nausea, epididymitis, benign prostatic hyperplasia, bladder irritability, reduced urine flow, priapism, premature epiphyseal closure (in children), and acne. Rare side effects include abnormal liver function, jaundice, liver tumors, greasy hair, oily skin, pruritus, rash, exanthema, urticaria at the injection site, and furunculosis. Local injection site reactions may also occur (**2**).

Unlike 17 α -alkylated AAS, such as methyltestosterone, nandrolone decanoate is not associated with liver toxicity (**17**).

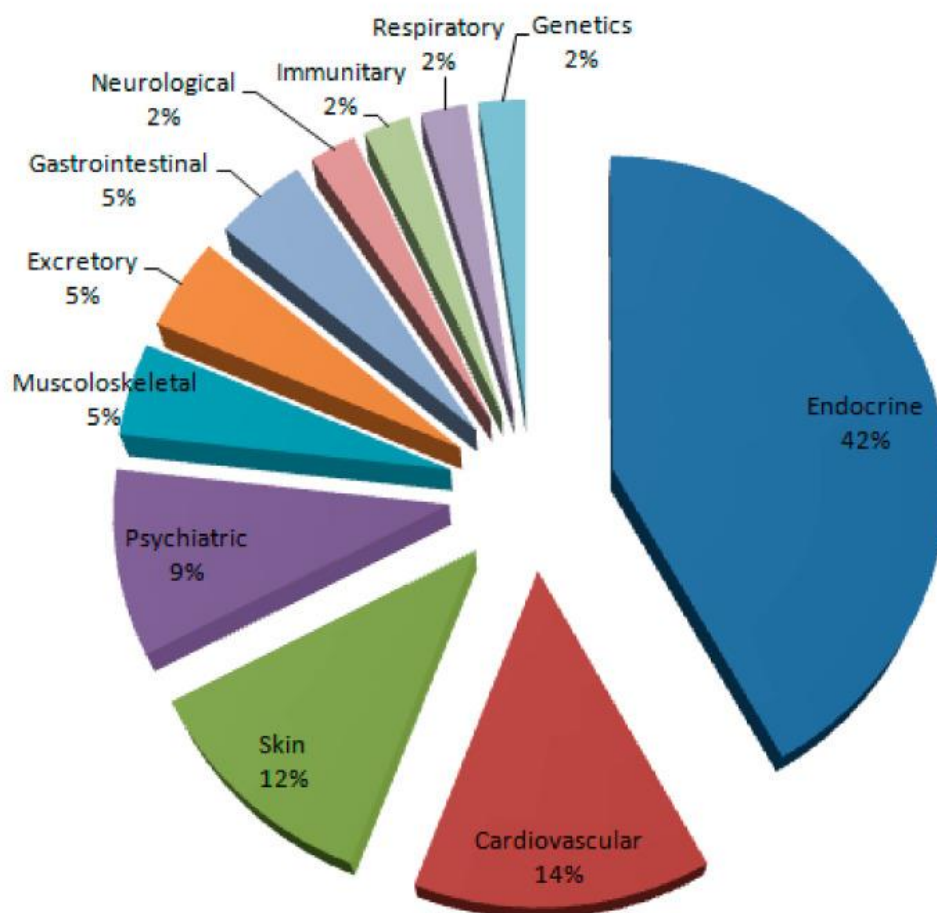


Fig. (3): The adverse effects reported. Endocrine, cardiovascular, skin and psychiatric disorders are the most reported (2).

The Most Common Systems Affected:

Endocrine and Genital Disorders

The most reported endocrine disorders were serum lipid alteration and virilization (for example, gynecomastia, voice pitch alteration). After a period of administration of AASs, several authors highlighted a significant increase of low-density lipoprotein (LDL) and decreasing high-density lipoprotein (HDL). Such effects and reversibility are dependent on dosage and treatment duration. It has been shown that high doses of AASs induce adverse effects by increasing plasma triglyceride levels and decreasing plasma HDL-C levels up to 70%, considered to provide anti-atherosclerotic protection (18),

Cardiovascular Disorders

Vasilaki et al. (19) observed focal fibrosis and inflammatory infiltrations of cardiac tissue after intramuscular and subcutaneous injection of nandrolone decanoate. These results were associated with increased Thiobarbituric acid-reactive species (TBARS) levels, distorted Myocardial Performance Index (MPI), rise in oxidative stress markers, and telomerase activity in cardiac tissue.

Skin Disorders

The most reported skin lesions were colored patches, acne, and itch disorders. Almainan and colleagues, in a study conducted on a group of gym athletes who were using a mix of several AASs, reported itching and the emergence of skin patches among other adverse reactions (20).

Psychiatric and Neurological Disorders

Long-term administration of AASs leads to several behavioral changes such as, concentration defects, anxiety, irritability, and even violence. In contrast, when the administration was discontinued, depression was the reported side effects. A common behavior found in AAS abusers is aggressiveness and this has been confirmed by several studies on animals (21).

Several studies carried on animals confirmed neurotoxic effects of AASs in the brain. Turillazzi and colleagues revealed the role played by oxidative stress, thus causing an apoptotic response in the rat brain after chronic treatment with nandrolone decanoate. The expression of serotonergic and noradrenergic neurotransmission was permanently influenced by chronic exposure (22).

Magnusson and colleagues proposed that administration of nandrolone to male rats may affect memory function via dynorphinergic actions. Both human and animal studies have shown dysfunction of visual-spatial memory after AAS use. (21).

Seitz and colleagues reported an increase in amygdala volume and reduced resting-state functional magnetic resonance imaging (MRI) coupling of the amygdala with cognitive control and memory regions in AAS abusers. The authors concluded that long-term AAS use might alter amygdala-related functional and structural brain networks (4).

Tachykinin levels were both affected by Chronic treatment with ND in brain areas connected with the control of emotional behavior such as depression, aggression, and reward (2).

Additionally, Selakovic and colleagues proposed the likelihood that variations in hippocampal parvalbumin interneurons (i.e., GABAergic system) may be involved in anxiousness provoked by ND abuse (23).

The androgen action is correlated to its ability to bind and activate AR. The immunoreactivity of substance P (SP), which is a peptidergic factor known to induce aggression in numerous brain regions, for example the amygdala, periaqueductal gray area, hypothalamus, and striatum, has been shown to increase after ND administration. ND has also been shown to react on the Substance P system at several levels, including receptor densities, enzymatic processing and peptide concentrations (2).

ND may induce its effect directly through AR, causing oxidative stress and different effects across the brain. Moreover, serotonin, glutamate, and dopamine systems, activation of gamma-aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) receptors as well as the activation of steroid receptors, such as estrogen, mineralocorticoid, progesterone, and glucocorticoid receptors, could all contribute to the altered behaviors described. Increased aggressive behavior has been shown in many studies but there is no univocal opinion of authors because of different methodological approaches (5).

Musculoskeletal Disorders

Mohamed& Mohamed (2022) reported hypertrophy of muscle fibers and disrupted striations with wide spacing between them on administration of nandrolone decanoate with noticeable degenerative changes in the quadriceps muscles of the adult male albino rats.

Excretory and Liver Disorders

Hepatotoxicity is one of the most frequent side effects of AAS abuse. AAS-induced hepatotoxicity has been hypothesized to be related to oxidative stress in hepatic cells. Indeed, because of AR activation an increase in reactive oxygen species can be observed due to the increase in mitochondrial β -oxidation. Moreover, antioxidant substances have a protective role against hepatotoxicity mediated by AASs. It has also been demonstrated that androgenic potency and metabolic resistance are positively linked to the degree of liver damage (24).

Conflicts of Interest: The authors declare no conflict of interest.

References

1. **William L. (2011)**: Anabolics. Molecular Nutrition Llc.; pp. 402–412, 193–194.
2. **Patanè FG, Liberto A, Maria Maglito AN, Malandrino P, Esposito M, Amico F, Cocimano G, Rosi GL, Condorelli D, Nunno ND, Montana A. (2020)**: Nandrolone Decanoate: Use, Abuse and Side Effects. *Medicina (Kaunas)*. Nov 11;56(11):606.
3. **McArdle, W. D., Katch, F. I., & Katch, V. L. (2020)**: *Exercise physiology: nutrition, energy, and human performance*. 9th edition Lippincott Williams & Wilkins.
4. **Monda V, Salerno M, Sessa F, Bernardini R, Valenzano A, Marsala G, Zammit C, Avola R, et al. (2018)**: Functional Changes of Orexinergic Reaction to Psychoactive Substances. *Mol. Neurobiol.*; 55: 6362–6368. doi: 10.1007/s12035-017-0865-z.
5. **Busardò, F. P., Frati, P., Sanzo, M. D., Napoletano, S., Pinchi, E., Zaami, S., & Fineschi, V. (2015)**: The impact of nandrolone decanoate on the central nervous system. *Current neuropharmacology*, 13(1), 122–131.
6. **Pan MM & Kovac JR. (2016)**: "Beyond testosterone cypionate: evidence behind the use of nandrolone in male health and wellness". *Transl Androl Urol.*; 5 (2): 213–9.
7. **Van Amsterdam J, Opperhuizen A, Hartgens F. (2010)**: Adverse health effects of anabolic–androgenic steroids. *Regul. Toxicol. Pharmacol.*; 57: 117–123.
8. **Kanayama, G., & Pope Jr, H. G. (2018)**: History and epidemiology of anabolic androgens in athletes and non-athletes. *Molecular and cellular endocrinology*, 464, 4-13.
9. **De Souza GL & Hallak J. (2011)**: Anabolic steroids and male infertility: A comprehensive review. *BJU Int*. 2011; 108: 1860–1865.
10. **Taylor & Francis (2000)**: Index Nominum 2000: International Drug Directory. pp; 716–717.
11. **Elks J. (2014)**: The Dictionary of Drugs: Chemical Data: Chemical Data, Structures and Bibliographies. Springer.; 660–672.
12. **Kicman AT. (2008)**: "Pharmacology of anabolic steroids". *Br. J. Pharmacol*; 154 (3): 502–21.
13. **Thomas JA. (2012)**: Drugs, Athletes, and Physical Performance. Springer Science & Business Media.; 27–29.
14. **Kalicharan, R.W.; Bout, M.R.; Oussoren, C.; Vromans, H. (2016)**: "Where does hydrolysis of nandrolone decanoate occur in the human body after release from an oil depot?". *International Journal of Pharmaceutics.*; 515 (1–2): 721–728.
15. **Dorfman RI. (2016)**: Steroidal Activity in Experimental Animals and Man. Elsevier Science; pp. 68–.
16. **Singh GK, Turner L, Desai R, Jimenez M, Handelsman DJ (2014)**: "Pharmacokinetic-pharmacodynamic study of subcutaneous injection of depot nandrolone decanoate using dried blood spots sampling coupled with ultrahigh pressure liquid chromatography tandem mass spectrometry assays". *J. Clin. Endocrinol. Metab.*; 99 (7): 2592–8.
17. **Hohl A. (2017)**: Testosterone: From Basic to Clinical Aspects. Springer.; pp. 394.
18. **Achar S, Rostamian A, Narayan SM**. Cardiac and Metabolic Effects of Anabolic-Androgenic Steroid Abuse on Lipids, Blood Pressure, Left Ventricular Dimensions, and Rhythm. *Am. J. Cardiol*. 2010; 106: 893–901.
19. **Vasilaki, F., Tsitsimpikou, C., Tsarouhas, K., Germanakis, I., Tzardi, M., Kavvalakis, M., ... & Tsatsakis, A. M. (2016)**: Cardiotoxicity in rabbits after long-term nandrolone decanoate administration. *Toxicology letters*, 241, 143-151.
20. **Almaiman AA, Almaiman SH, Elagamy EI, Al Wutayd O, Almarzuqi M, Alzunaidi R, Alhatlani S, Eid EE (2019)**: Side effects of anabolic steroids used by athletes at Unaizah Gyms, Saudi Arabia: A pilot study. *J. Sports Med Phys. Fit.*; 59: 489–495.
21. **Bertozi G, Salerno M, Pomara C, Sessa F. (2019)**: Neuropsychiatric and Behavioral Involvement in AAS Abusers. A Literature Review. *Medicina.*; 55: 396.
22. **Rainer Q, Speziali S, Rubino T, Dominguez-Lopez S, Bambico FR, Gobbi G, Parolaro D. (2014)**: Chronic nandrolone decanoate exposure during adolescence affects emotional behavior and monoaminergic neurotransmission in adulthood. *Neuropharmacology.*; 83: 79–88.
23. **Selakovic D, Joksimovic J, Zaletel I, Puskas N, Matovic M, Rosic G. (2017)**: The opposite effects of nandrolone decanoate and exercise on anxiety levels in rats may involve alterations in hippocampal parvalbumin–positive interneurons. *PLoS ONE.*; 12: e0189595.
24. **Solimini R, Rotolo MC, Mastrobattista L, Mortali C, Minutillo A, Pichini S, Pacifici I, Palmi I. (2017)**: Hepatotoxicity associated with illicit use of anabolic androgenic steroids in doping. *Eur. Rev. Med. Pharmacol. Sci*; 21(Suppl. 1):7–16.