# Effect of Anabolic Steroids on Muscle Mass and Fertility in the Male Albino Rat

## Thesis

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# تأثير الستيرويد البنائى على الكتلة العضلية وعلى الخصوبة في ذكر الجرذ الأبيض

رسالة

توطئة للحصول على درجة الدكتوراه في العلوم الطبية الأساسية (التشريح و الأجنة)

مقدمة من


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# List of Abbreviations

**AAS : Androgenic Anabolic Steroid.**

**AASs : Androgenic Anabolic Steroids.**

**A.R.E : Arab Republic of Egypt.**

**BMR : Basal Metabolic Rate.**

**CO. : Company.**

**FSH : Follicle Stimulating Hormone.**

**GH : Growth hormone.**

**GnRh : Gonadotrophin Releasing hormone.**

**HPG axis : Hypothalamic Pituitary Gonadal axis.**

**Hx&E : Hematoxylin and Eosin.**

**IGF1 : Insulin Growth Factor1.**

**LH : Leutinizing Hormone.**

**NA : Norandrosterone.**

**ND : Nandrolone Decanoate.**

**NE : Noretiocholanolone.**

**PMC : Peritubular Myoid Cell.**

**rER : rough Endoplasmic Reticulum.**

**sER : smooth Endoplasmic Reticulum.**

**SCs : Satellite cells.**

**SPSS : Statistical Package scientific Significance.**

**US : United State.**

**USC : United State Code.**

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# Introduction

AAS are synthetic versions of the naturally occurring male sex hormone (**testosterone)**. They are more properly called **anabolic-androgenic steroids (AASs),** because they have anabolic and masculinizing (androgenic) effects. The masculinizing effects of testosterone cause male characteristics to appear during puberty in boys, such as enlargement of the penis, hair growth on the face and pubic area, muscular development, and deepened voice. Females also produce natural testosterone, but ordinarily in much smaller amounts than males ***(Wright & Cowart, 1990).***

AASs are used in various medical conditions as cachexia, anemia, and chronic disease states (***Kicman, 2008)***.For many years, androgenic-anabolic steroids have been popular among athletes both for performance improvement and for aesthetic reasons (***Hartgens and Kuipers, 2004***). AAS have been abusively used by many men and women, athletes and nonathletes to increase muscle mass and strength ***(Gerez et al., 2005)***. However, there is no compelling evidence that limb muscles undergo hypertrophy in response to anabolic steroids **(*Jarow and Lipshultz, 1990*).**

Although AAS have been banned in organized sports for nearly thirty years, their use remains one of the main health-related problems in sports today because of their availability and low price (***Karila, 2004***).

The abuse of these compounds by athletes could be risky and dangerous as it affects the mental state and several systems (***Tahtamouni et al., 2010)***. One of the most pronounced effects of AAS abuse is the negative impact on the hypothalamus-pituitary-gonadal axis (***Takahashi et al., 2004***). When a male takes steroids, the pituitary gland detects the sudden high quantity of anabolic steroids and sends chemical signals to shut down testosterone production in the testes. The longer a person takes anabolic steroids, the longer the testes remain inactive. The sperm cells begin to have abnormal shapes, and are fewer in number ***(Knuth et al., 1989).*** If AAS abuse continues long enough, the male becomes infertile ***(Yesalis et al., 1989).*** The testes of male athletes who have been stacking and cycling steroids for years decrease in size. If the adult male stops, it may take four months to a year or more to regain normal sperm cell shape and fertility ***(Knuth et al., 1989).***

Due to widespread abuse, many side-effects of AAS abuse may turn out to be significant risk factors when considering public health (***Karila, 2004)***. Furthermore, the mechanism of action of AAS is not completely understood and is still subject to research ***(Hartgens and Kuipers, 2004)***. Therefore the effect of nandrolone decanoate on both muscle and testis of the rat will be studied. Furthermore, the effects of its withdrawal will be investigated as a controversy exists regarding improvement of the side effects produced by AAS upon withdrawal ***(Karbalay-Doust et al., 2007*)**.

# Aim of the Work

The aim of this work was to study the effect of nandrolone decanoate, one of the anabolic steroids, on muscle mass and fertility in the male albino rat. Also, to clarify the reversibility of any changes caused by these compounds after drug discontinuation for twelve weeks.

# Anabolic Androgenic Steroids

**Anabolic androgenic steroids** (**AASs**) are synthetic derivatives of the male hormone testosterone ***(Hartgens and Kuipers, 2004)***. These drugs mimic the effects of the male sex hormones testosterone and dihydrotestosterone. They increase protein synthesis within cells, which results in the buildup of cellular tissue (anabolism), especially in muscles. Anabolic steroids also have androgenic and virilizing properties, including the development and maintenance of masculine characters such as the growth of the vocal cords, testicles, and body hair (secondary sexual characters) ***(Deidre, 2005).***

With structural modifications of testosterone, the anabolic properties (tissue building) of (AAS) can be enhanced, while (sex-linked) properties can be minimized. However, no steroid has eliminated the androgenic effects because the so-called androgenic effects are really anabolic effects in sex-linked tissues. The effects of male hormones on accessory sex glands, and genital hair growth, are anabolic processes in those tissues. The steroids with the most potent anabolic effect are also those with the greatest androgenic effect ***(Kicman, 2008).***

The androgenic: anabolic ratio of an AAS is an important factor when determining the clinical application of these compounds. Compounds with a high ratio of androgenic to

anabolic effects are the drug of choice in androgen-replacement therapy (e.g. treating hypogonadism in males), whereas compounds with a reduced androgenic: anabolic ratio are preferred for anemia, osteoporosis, and to reverse protein loss following trauma, surgery or prolonged immobilization. Determination of androgenic: anabolic ratio is typically performed in animal studies, which has led to the marketing of some compounds claimed to have anabolic activity with weak androgenic effects. This disassociation is less marked in humans, where all anabolic steroids have significant androgenic effects ***(Chrousos, 2006).***

## Mechanism of action of androgenic anabolic steroids:

Anabolic steroids are membrane permeable and influence the nucleus of cells by direct action. When they penetrate the membrane of the target cell and bind to an androgen receptor located in the cytoplasm of that cell, the compound hormone-receptor diffuses into the nucleus, where it alters the processes that send signals to other parts of the cell (***Lavery and McEwan, 2005).*** Different types of anabolic steroids bind to the androgen receptor with different affinities, depending on their chemical structure ***(Hartgens and Kuipers, 2004).*** Some anabolic steroids such as methandrostenolone bind weakly to this receptor ***in vitro***, but still exhibit androgenic effects ***in vivo (Roselli, 1998).*** Steroid hormones work by stimulation of

receptor molecules in muscle cells, which activate specific genes to produce proteins. They also affect the activation rate of enzyme systems involved in protein metabolism, thus enhancing protein synthesis and inhibiting protein degradation (called an anti-catabolic effect). The effectiveness of anabolic steroids is dependent upon unbound receptor sites in muscle. Intense strength training may increase the number of unbound receptor sites. This would increase the effectiveness of anabolic steroids ***(Bahrke et al., 1992).***

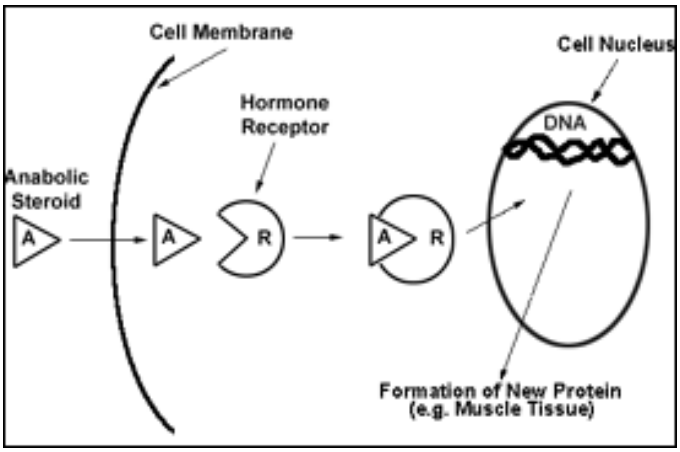


**Diagram (1):** How a Steroid Hormone Works ***(cited from Fahey, 1998).***

Many athletes claimed that anabolic steroids help them train harder and recover faster. They added that they had difficulty making progress (or even holding onto the gains) when they were off the drugs. Anabolic steroids may have an anti-catabolic effect. This means that the drugs may prevent muscle catabolism that often accompanies intense exercise