جامعة
بنغازي الحديثة

مجلة جامعة بنغازي الحديثة للعلوم والدراسات الإنسانية

مجلة علمية الكترونية محكمة

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العـــدد الرابع

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شروط كتابة البحث العلمي في مجلة جامعة بنغازي الحديثة للعلوم والدراسات الإنسانية

1- الملخص باللغة العربية وباللغة الانجليزية (150 كلمة).
2- المقدمة، وتشمل التالي:
- ❖ نبذة عن موضوع الدراسة (مدخل).
- ❖ مشكلة الدراسة.
- ❖ أهمية الدراسة.
- ❖ أهداف الدراسة.
- ❖ المنهج العلمي المتبع في الدراسة.

3- الخاتمة. (أهم نتائج البحث - التوصيات).
4- قائمة المصادر والمراجع.
5- عدد صفحات البحث لا تزيد عن (25) صفحة متضمنة الملاحق وقائمة المصادر والمراجع.

القواعد العامة لقبول النشر

1. تقبل المجلة نشر البحوث باللغتين العربية والانجليزية؛ والتي تتوافر فيها الشروط الآتية:

- أن يكون البحث أصيلاً، وتتوافر فيه شروط البحث العلمي المعتمد على الأصول العلمية والمنهجية المتعارف عليها من حيث الإحاطة والاستقصاء والإضافة المعرفية (النتائج) والمنهجية والتوثيق وسلامة اللغة ودقة التعبير.
- ألا يكون البحث قد سبق نشرة أو قُدم للنشر في أي جهة أخرى أو مستل من رسالة أو اطروحة علمية.
- أن يكون البحث مراعياً لقواعد الضبط ودقة الرسوم والأشكال - إن وجدت - ومطبوعاً على ملف وورد، حجم الخط (14) وبخط (Arial 'Body') للغة العربية. وحجم الخط (12) بخط (Times New Roman) للغة الإنجليزية.
- أن تكون الجداول والأشكال مدرجة في أماكنها الصحيحة، وأن تشمل العناوين والبيانات الإيضاحية.
- أن يكون البحث ملتزما بدقة التوثيق حسب دليل جمعية علم النفس الأمريكية (APA) وتثبيت هوامش البحث في نفس الصفحة والمصادر والمراجع في نهاية البحث على النحو الآتي:
- أن تُثبت المراجع بذكر اسم المؤلف، ثم يوضع تاريخ نشرة بين حاصرتين، ويلي ذلك عنوان المصدر، متبوعاً باسم المحقق أو المترجم، ودار النشر، ومكان النشر، ورقم الجزء، ورقم الصفحة.
- عند استخدام الدوريات (المجلات، المؤتمرات العلمية، الندوات) بوصفها مراجع للبحث: يُذكر اسم صاحب المقالة كاملاً، ثم تاريخ النشر بين حاصرتين، ثم عنوان المقالة، ثم ذكر اسم المجلة، ثم رقم المجلد، ثم رقم العدد، ودار النشر، ومكان النشر، ورقم الصفحة.

2. يقدم الباحث ملخص باللغتين العربية والانجليزية في حدود (150 كلمة) بحيث يتضمن مشكلة الدراسة، والهدف الرئيسي للدراسة، ومنهجية الدراسة، ونتائج الدراسة. ووضع الكلمات الرئيسية في نهاية الملخص (خمس كلمات).

3. تحتفظ مجلة جامعة بنغازي الحديثة بحقها في أسلوب إخراج البحث النهائي عند النشر.

إجراءات النشر

ترسل جميع المواد عبر البريد الالكتروني الخاص بالمجلة جامعة بنغازي الحديثة وهو كالتالي:

- ✓ يرسل البحث الكترونياً (Word + Pdf) إلى عنوان المجلة info.jmbush@bmu.edu.ly او نسخة على CD بحيث يظهر في البحث اسم الباحث ولقبة العلمي، ومكان عملة، ومجاله.
- ✓ يرفق مع البحث نموذج تقديم ورقة بحثية للنشر (موجود على موقع المجلة) وكذلك ارفاق موجز للسيرة الذاتية للباحث إلكترونياً.
- ✓ لا يقبل استلام الورقة العلمية الا بشروط وفورمات مجلة جامعة بنغازي الحديثة.
- ✓ في حالة قبول البحث مبدئياً يتم عرضة على مُحكِّمين من ذوي الاختصاص في مجال البحث، ويتم اختيارهم بسرية تامة، ولا يُعرض عليهم اسم الباحث أو بياناته، وذلك لإبداء آرائهم حول مدى أصالة البحث، وقيمته العلمية، ومدى التزام الباحث بالمنهجية المتعارف عليها، ويطلب من المحكم تحديد مدى صلاحية البحث للنشر في المجلة من عدمها.
- ✓ يُخطر الباحث بقرار صلاحية بحثه للنشر من عدمها خلال شهرين من تاريخ الاستلام للبحث، وبموعد النشر، ورقم العدد الذي سينشر فيه البحث.
- ✓ في حالة ورود ملاحظات من المحكِّمين، تُرسل تلك الملاحظات إلى الباحث لإجراء التعديلات اللازمة بموجبها، على أن تعاد للمجلة خلال مدة أقصاها عشرة أيام.
- ✓ الأبحاث التي لم تتم الموافقة على نشرها لا تعاد إلى الباحثين.
- ✓ الأفكار الواردة فيما ينشر من دراسات وبحوث وعروض تعبر عن أراء أصحابها.
- ✓ لا يجوز نشر إي من المواد المنشورة في المجلة مرة أخرى.
- ✓ يدفع الراغب في نشر بحثه مبلغ قدره (400 د.ل) دينار ليبي إذا كان الباحث من داخل ليبيا، و (200 $) دولار أمريكي إذا كان الباحث من خارج ليبيا. علماً بأن حسابنا القابل للتحويل هو: **(بنغازي – ليبيا - مصرف التجارة والتنمية، الفرع الرئيسي - بنغازي، رقم 001-225540-0011. الاسم (صلاح الأمين عبدالله محمد)**.
- ✓ جميع المواد المنشورة في المجلة تخضع لقانون حقوق الملكية الفكرية للمجلة.

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The Effects of Testosterone on Body Weight and Blood Picture in Male Rabbits

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ABSTRACT.

This study was carried out to investigate the effect of the male hormone testosterone (T) on weight and blood picture of male rabbits. Fifteen (15) adult male rabbits were weighed and divided into 3 groups: a control group (received 100 µl of sesame oil), a low dose group (received 6 mg T/ kg b. w.), and a high dose group (received 12 mg/kg b. w.). The rabbits were injected intramuscularly once a week for 6 weeks. After the end of the injection period, the rabbits were weighed, slaughtered and blood samples collected for analysis. Injection of T caused significant increases in the levels of T and growth hormone in the sera of treated animals. The hormone also caused significant increases in the weights of treated rabbits. The red blood corpuscles count, the hemoglobin concentration, the percent hematocrit and the platelets count were found to significantly increase with the injection of T. The hormone had no significant effect on the mean corpuscular volume, the mean corpuscular hemoglobin, the mean corpuscular hemoglobin concentration and white blood cells. It is concluded that the increases in red blood corpuscles could have a significant effect on the viscosity of the blood, which could also have an effect on the heart function.

Keywords: Testosterone, Body Weight, Blood Picture, Rabbits.

INTRODUCTION.

Testosterone is the primary male sex hormone and an anabolic steroid. In men, testosterone plays a key role in the development of male reproductive tissue such as the testes and prostate, as well as promoting secondary sexual characteristics such as increased muscle and bone mass and the growth of body hair **(Mooradian *et al.*, 1987)**. In addition, testosterone is essential for health and well-being **(Bassil *et al.*, 2009)** and for the prevention of osteoporosis **(Tuck and Francis, 2009)**. Insufficient levels of testosterone in men may lead to abnormalities including frailty and bone loss. Testosterone is also used as medication to treat male hypogonadism and certain types of cancer **(Drazer and Stadler, 2016)**. Since testosterone levels gradually decrease as men age, synthetic testosterone is sometimes prescribed to older men to counteract this deficiency. The use of testosterone and related steroids is a widespread phenomenon among top athletes, amateurs and a large part of the population who simply desire to improve their appearance. The popularity of testosterone and related steroids among drug users is due to the powerful effects of these substances on muscle strength and mass. The anabolic testosterone is taken by intramuscular injection and as gels and creams. These drugs are used to increase lean body mass, to decrease fat mass, to enhance performance, to sustain intensive training periods and to improve the appearance **(Yesalis, 1993; Hartgens and Kuipers, 2004)**. However, anabolic drugs have been associated with a wide range of adverse effects including deleterious changes in risk factors associated with cardiovascular disease, alteration in liver structure and function, and in the reproductive system and changes in behavior **(Wilson, 1988)**. Therefore, for these reasons, this hormone was tested with two different doses to investigate its effect on weight and blood picture of male rabbits.

MATERIALS AND METHODS.

Animals:

Twelve-weeks old, healthy Egyptian male rabbits (total 15) (weighing between 1.2-1.6 kg) were obtained from a local breeder and were maintained in individual cages in the animal care center of the faculty of Veterinary medicine. The animals were maintained under normal temperature and light cycles. The rabbits were given water and food *ad libitum*. The animals were kept and maintained under these conditions for 4 weeks prior to the experiment.

Chemicals:

Testosterone (cidotestone, 250 mg/ml ampoule for intramuscular injection, made by Chemical Industries Development, Egypt) was obtained from a local pharmacy. Sesame oil (Almadina Company, Ajdabia-Libya) was also obtained from a local pharmacy.

Experimental procedure:

The rabbits were weighed and divided randomly into 3 groups (5 rabbits in each group): 1- control group (received 100 µl sesame oil), 2- low dose group (received 6 mg testosterone/kg b. w.), 3- high dose group (received 12 mg testosterone/kg b. w.) **(Gui *et al.*, 2008; Zhao *et al.*, 2013)**. The rabbits were injected with testosterone intramuscularly using 1 ml syringe once a week for 6 weeks **(Aydilek and Aksakal, 2005; Zhao *et al.*, 2013)**.

After the end of the 6 weeks period, the rabbits were weighed, slaughtered and blood samples were taken from the 3 groups. From each rabbit, blood samples (3 ml) were collected

into ethylene diamine tetra acetic acid (EDTA) tubes for hematological parameters analysis, and (4 ml) into tubes without EDTA for hormonal parameters.

Hematological parameters:

Hematological parameters including white blood cells (WBC), red blood cells (RBC), hematocrit (HCT), Hemoglobin (HGB), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and platelets were evaluated using an automatic blood cell analyzer (XP-300 Automated Hematology Analyzer, Sysmex America, Inc.).

Hormonal parameter:

Blood samples were centrifuged at 4000 rpm, for 5 minutes and the serum was used to measure the levels of the following hormones:

Growth hormone (GH) and testosterone (T) which were measured automatically using Elecsys 2010 (RD/Hitachi Immunoassay System 2010 from Roche Diagnostics/Hitachi, Japan).

Statistical analysis:

Statistical analysis was performed using a computer run package (Graph Pad Prism 7). One way ANOVA followed by Tukey's HSD test was performed to show the statistical significance among the means of the groups. Results were expressed as mean ± Standard error of the mean (SEM), N = 5. P-value below 0.05 was considered to be statistically significant.

RESULTS.

None of the rabbits in this study exhibited overt clinical signs of toxicity in response to treatment with testosterone.

The injection of the rabbits with testosterone (T) resulted in a significant increase in the level of this hormone in the serum of the treated animals in comparison with the sesame oil injected controls. The results are shown in **figure 1**. This figure clearly shows a huge significant difference ($p < 0.0001$) between the control group (1.362 ± 0.78 U/ml) and the group treated with 6 mg T (12.37 ± 1.90 U/ml) and the group treated with 12 mg T (14.82 ± 0.12 U/ml). Even though the group treated with 12 mg T had slightly higher level of T than the 6 mg T treated group, this increase was not significantly different.

Figure 2 shows a comparison between the weights of the 3 groups at the beginning of the experiment and after the end of the 6 week treatment. There were no significant differences between the mean weights of the 3 groups at the beginning of the experiment. From this figure, it is clear that there were significant increases in the weights of the 3 groups after 6 weeks. The mean weight of the control group increased from 1.38 ± 0.06 Kg to 1.8 ± 0.05 ($p = < 0.0001$) and that of the 6 mg T treated group increased from 1.38 ± 0.02 Kg to 2.1 ± 0.07 ($p < 0.0001$). The mean weight of the 12 mg T treated group also increased. This increase was from 1.52 ± 0.02 Kg to 2.24 ± 0.02 Kg ($p < 0.0001$). However, there were significant increases in the weights after treatment of the 6 mg T and the 12 mg T treated groups when compared with the weight of the control group after treatment. But even though the weight of the 12 mg T treated group was slightly higher than that of the 6 mg T treated group, this increase was not statistically significant.

The results, however, may indicate that this effect is dose dependent. Testosterone also has an effect on growth hormone (GH) **(figure 3)**. There was an almost 60 % increase in the mean level of GH in the serum of the 6 mg T treated group (0.130 ± 0.022 U/ml) in comparison with that in the control group (0.052 ± 0.02). This, however, was not statistically significant ($p = 0.051$). The 12 mg T caused an increase of about 65 % in the mean level of GH (0.151 ± 0.020 U/ml) which was statistically different ($p = 0.014$) when compared with the control but not different ($p = 0.753$) when compared with that of the 6 mg T treated group.

The results of the effect of T on the red blood cells (RBC) count in the control and treated rabbits are shown in **figure 4**. The mean RBC count in the control group was 4.73 ± 0.13 x 10^6/ml. This was slightly lower than the normal range (5.1 ± 7.9 x 10^6/ml) reported by **Cooke (2000)**. However, when the rabbits were injected with the 6 mg T, the count increased to 5.11 ± 0.20 x 10^6/ml, though this increase was not statistically significant when compared with that of the control. The 12 mg T, on the other hand, increased the mean RBC count to 5.90 ± 0.20 x 10^6/ml. This count was statistically higher than that from that of the control group ($p = 0.0019$) and that of the 6 mg T treated group ($p = 0.026$). This increase appears to be dose dependent.

The mean hemoglobin (HGB) concentration of the control group was 10.9 ± 0.22 g/dl. This was within the normal range (10-17 g/dl) reported by **Cooke (2000)**. The mean HGB concentration of the 6 mg T treated group was 10.96 ± 0.20 g/dl. This was not statistically different ($p > 0.05$) from that of the control group. However, the 12 mg T increased the mean HGB concentration to 13.04 ± 0.54 g/dl. This concentration was statistically higher than that of the control group ($p = 0.0031$) and of the 6 mg T treated group ($p = 0.0039$). The results are shown in **figure 5**.

The results of the effect of testosterone on the percentage of hematocrit (HCT) are represented in **figure 6**. From this figure, it is clear that there was no significant difference ($p = 0.85$) between the mean percent HCT in the control group (33.46 ± 1.2) and that of the 6 mg T treated group (34.44 ± 1.1). The 12 mg T increased the mean percent HCT to 40.66 ± 1.6. This percentage was statistically higher than that of the control group ($p = 0.0057$) and that of the 6 mg T treated group ($p = 0.0147$).

The results of the effect of testosterone on the MCV, MCH and MCHC are shown in **figures 7, 8 and 9**, respectively. The means of the controls in these figures are within the ranges reported by **Cooke (2000)**. From the results of these figures it was clear that the testosterone had no statistically significant effect on these parameters.

The mean count of total white blood cells (WBC) was 10.24 ± 0.93 x 10^3/µl. This value is within the normal range reported by **Cooke (2000)**. This number increased slightly to 10.4 ± 0.42 x 10^3/µl in the 6 mg T treated group, but the 12 mg T caused a slight decrease (9.84 ± 0.90) in the mean total number of WBC. However, these changes are not statistically different from the control group. The results are shown in **figure 10**.

With regard to platelets, even though the mean count of platelets (199.2 ± 30.64 x 10^3/µl) of the control group was below the range (240-600) reported by **Cooke (2000)**, the 6 mg T increased the mean platelets count to 276.6 ± 18.8 x 10^3/µl; however, this increase was not significantly different from that of the control group. Testosterone at 12 mg, however, raised the mean platelet count to 401.6 ± 53.21 x 10^3/µl. This number was statistically different ($p = 0.0059$) from that of the control group, but not different from that of the 6 mg T

treated group (p = 0.081). From **figure 11**, it appears that there is a rise in the total count of platelets with the treatments and this increase appears to be dose dependent.

DISCUSSION.

In this experiment, the testosterone concentrations used were 6 mg/kg and 12 mg/kg, based on the study by **Gui *et al*. (2008)** who used these concentrations to study the effect of testosterone on blood lipids in castrated rabbits. These doses caused a huge increase in the level of testosterone in the serum of treated rabbits. The doses used in this experiment have caused a dose-dependent increase in body weight. This is expected since the main reason behind the popularity of testosterone among drug users is its effects on athletic performance and on muscle size. Administration of replacement doses of testosterone to healthy young men **(Brodsky *et al*., 1996; Katznelson *et al*., 1996; Bhasin *et al*., 1997; Snyder *et al*., 2000; Wang *et al*., 2000)** and older men with low testosterone **(Tenover, 1992; Morley *et al*., 1993; Snyder *et al*., 1999; Kenny *et al*., 2001)** and human immunodeficiency virus (HIV)-infected men with low testosterone levels **(Bhasin *et al*., 2000)** and administration of supraphysiological doses to eugonadal men **(Bhasin *et al*., 1996; Bhasin *et al*., 2001)** increases muscle size. Studies had also shown that serum testosterone levels were positively correlated with body weight, lean body mass and muscle mass **(Griggs *et al*., 1989; Welle *et al*., 1992; Grinspoon *et al*., 1996; Wang *et al*., 1996)**. It is believed that testosterone supplementation increases muscle mass by inducing muscle fiber hypertrophy **(Bhasin *et al*. 2003)**. To evaluate whether testosterone-induced increase in muscle size is due to muscle fiber hypertrophy, **Sinha-Hikim *et al*. (2002)** treated young eugonadal men with monthly injections of a substance to suppress endogenous testosterone secretion and weekly injections of graded doses of testosterone for 20 weeks. Muscle biopsies were obtained before and after 20 weeks.

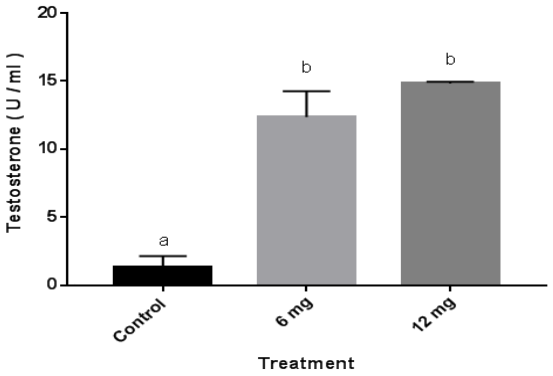

Figure 1: The concentration of testosterone in the serum of the control group injected with sesame oil and in the rabbits treated with testosterone (6 mg/kg and 12 mg/kg) once a weak for 6 weeks. Results are mean ± SEM (n = 5). Similar letters indicate no significant difference, while different letters indicate significant difference between the means.

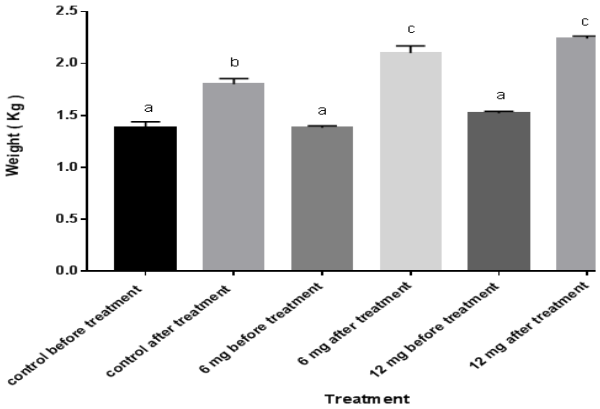

Figure 2: Mean weights of control rabbits and rabbits treated with testosterone (6 mg and 12 mg / kg) before and after the end of the 6 week treatment period. Results are mean ± SEM (n = 5). Similar letters on the bars indicate no significant difference. Different letters indicate significant difference.

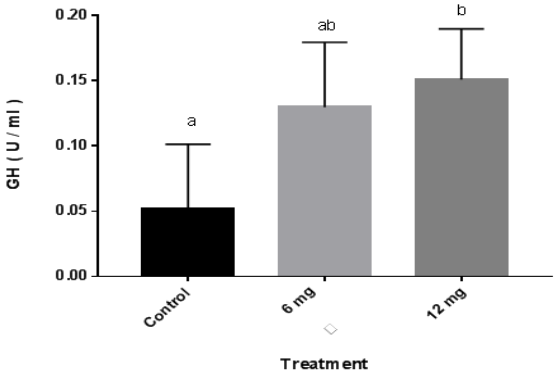

Figure 3: The level of growth hormone (GH) in the serum of the control and testosterone (6 mg/kg and 12 mg/kg) treated rabbits. The results are mean ± SEM (n = 5). Different letters indicate significant difference between the means. Similar letters indicate no significant differences between the means.

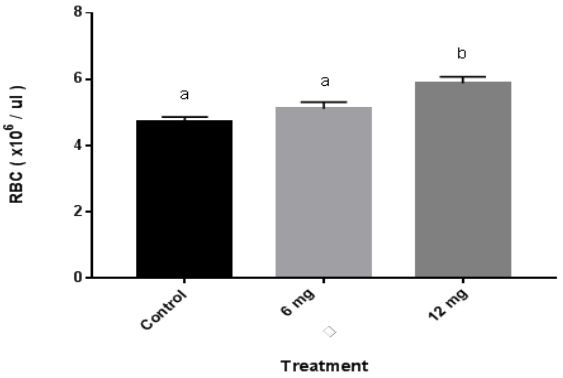

Figure 4: Means of red blood corpuscle counts (RBC) from the control rabbits and the rabbits treated with two different doses of testosterone (6 mg and 12 mg / kg) for 6 weeks. Different letters indicate significant differences between the means ($p < 0.05$). Similar letters indicate no differences.

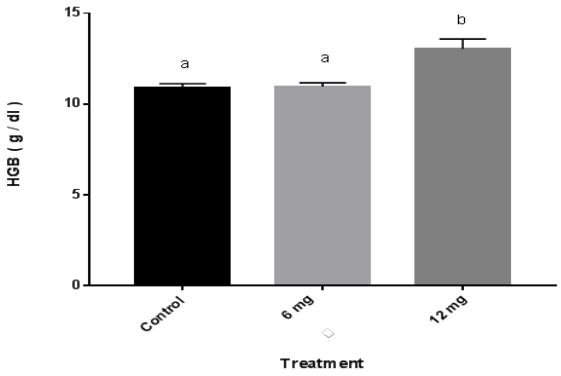

Figure 5: The mean concentration of hemoglobin (HGB) in the control rabbits and the testosterone (6 mg and 12 mg) treated rabbits. Similar letters indicate no significant difference between the means. Different letters indicate significant difference.

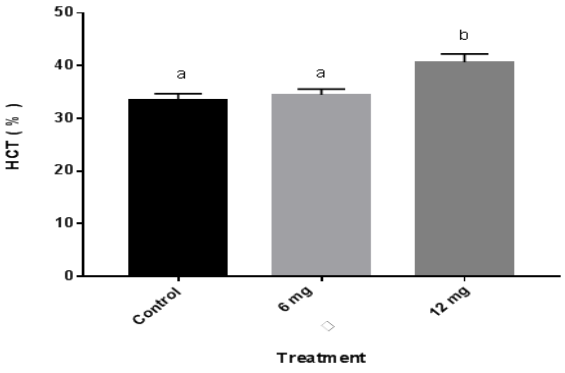

Figure 6: The mean percent of hematocrit (HCT) from the non- treated (control) rabbits and the testosterone (6 mg and 12 mg/kg) treated rabbits.The results are mean ± SEM (n = 5). Similar letters indicate no significant differences between the means. Different letters indicate significant differences.

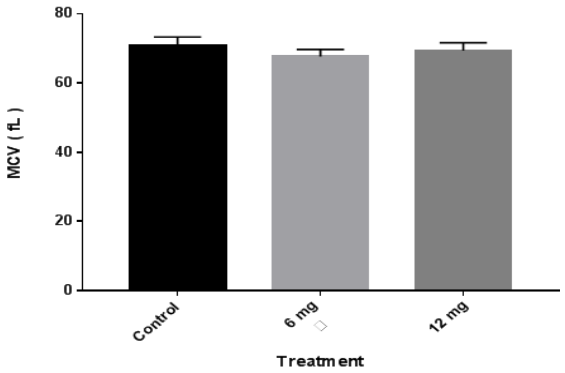

Figure 7: The mean corpuscular volume (MCV) of control rabbits and those treated with testosterone. Results are mean ± SEM (n = 5). No significant differences between the means.

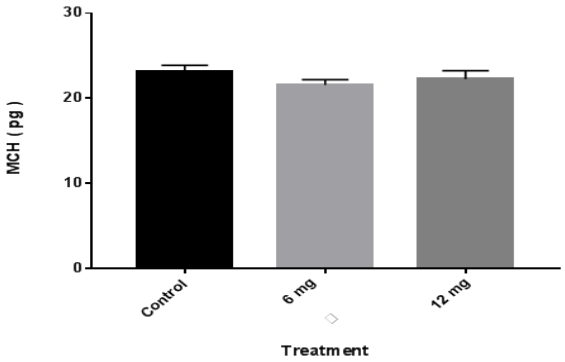

Figure 8: The mean corpuscular hemoglobin (MCH) of the testosterone treated rabbits (6 mg/kg and 12 mg/kg) and the control rabbits after 6 weeks treatment period. Results are mean ± SEM (n = 5). No significant differences between the means.

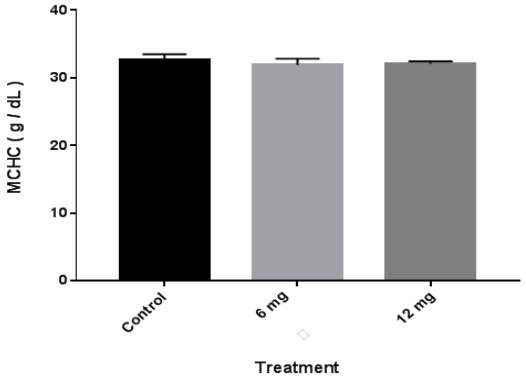

Figure 9: The mean corpuscular hemoglobin concentration (MCHC) of control and testosterone (6 mg/kg and 12 mg/kg) treated rabbits after 6 weeks treatment period. Results are mean ± SEM (n = 5). No significant differences between the means.

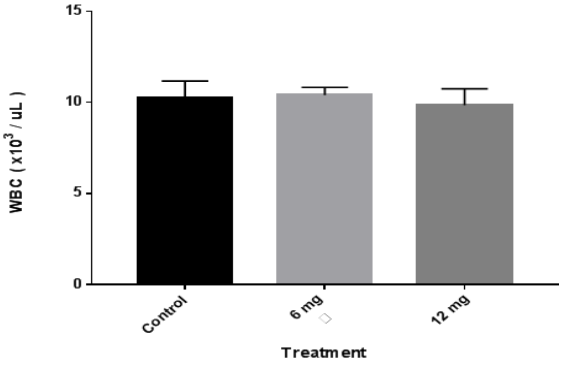

Figure 10: The mean white blood cells (WBC) count of control and testosterone (6 mg/kg and 12 mg/kg) treated rabbits after 6 week treatment period. Results are mean ± SEM (n = 5). No significant differences between the means.

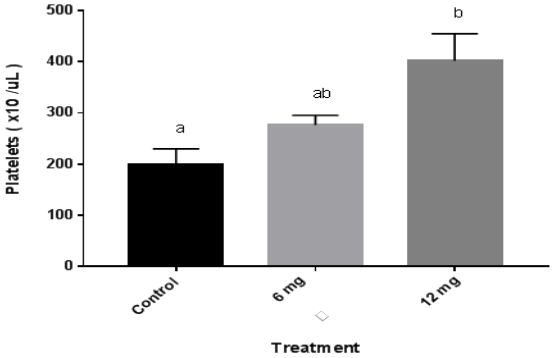

Figure 11: Platelets count in the blood of control and testosterone (6 mg/kg and 12 mg/kg) treated rabbits after 6 weeks of treatment. Results are mean ± SEM (n = 5). Similar letters indicate no significant difference between the means. Different letters indicate significant differences.

They found that the muscle volume increased in proportion to the administered dose and the cross-sectional areas of type I and type II fibers also increased in direct correlation with the testosterone dose. The relative proportions of type I and type II fibers did not change significantly after treatment in any group. Thus, the increase in muscle volume in healthy

eugonadal men treated with graded doses of testosterone is due to concentration-dependent hypertrophy of both type I and type II muscle fibers **(Bhasin *et al*., 2001; Sinha-Hikim *et al*., 2002)**. The growth of rabbits treated with testosterone could also be due to the enhanced secretion of growth hormone by testosterone. In this study the testosterone treated rabbits had higher levels of growth hormone than the control group. Testosterone was found to increase growth hormone secretion in prepubertal growth hormone deficient male patients **(Silva *et al*., 1992)** and to stimulate growth hormone secretion in adult male rhesus monkey **(Rizvi *et al*., 2000)**. Testosterone administration to pubertal boys increased spontaneous growth hormone secretion **(Eakman *et al*., 1996)**. Testosterone caused increased release of growth hormone in patients with anorchia and in boy with delayed puberty **(Illig and Prader, 1970)**. This increase appeared 2 days after a single injection of testosterone, and became still higher after 2-3 months of full replacement therapy. In a study evaluating the modifying effect of growth hormone on the growth-promoting action of testosterone in boys at pubertal bone age, **Daniel *et al.* (1979)** concluded that testosterone exerts its full growth promoting action only in the presence of normal endogenous growth hormone secretion. Testosterone at 0.1 mg/day was found to enhance the growth-promoting effect of growth hormone on muscle of hypophysectomized male rats **(Scow and Hagan, 1965)**. **Brill *et al*. (2002)** examined the combined effect of growth hormone and testosterone in healthy older men. They found that combining both hormones together increased the fat-free mass. **Birzniece *et al.* (2011)** concluded that testosterone stimulates protein anabolism by reducing protein breakdown and oxidation only in the presence of growth hormone and that the liver is the primary site of this hormone interaction. Testosterone replacement in hypopituitary adults increased circulating insulin-like growth factor I (IGF-I), only during concomitant administration of growth hormone **(Gibney *et al*., 2003)**. These authors stated that testosterone and growth hormone exerted independent and additive effects to increase protein synthesis, and concluded that testosterone enhances the effect of growth hormone to increase IGF-I, but exerts a protein anabolic effect that is independent of GH action.

In this study testosterone caused an increase in the RBC count , the percentage of hematocrit, and the concentration of hemoglobin. These increases appeared to be dose-dependent. Similar results were also reported in humans by **Snyder *et al*. (2000), Bhasin *et al.* (2005), Calof *et al*. (2005), Coviello *et al*. (2008), Bachman *et al*. (2014), Beggs *et al*. (2014)** and in castrated rabbits by **Zhao *et al.* (2013)**, and in mice by **Guo *et al*. (2013 a and b)**. It appears that increased red blood cells (erythrocytosis) is the most common adverse event associated with testosterone therapy in clinical practice and in testosterone trials **(Bachman *et al*., 2014)**. **Beggs *et al*. (2014)** found that testosterone alters iron metabolism and stimulates red blood cell production independently of dihydrotestosterone. **Bachman *et al*. (2014)** proposed that testosterone stimulates erythrocytosis by stimulating erythropoietin (EPO) and by increasing iron utilization for erythropoiesis. However, human studies have not provided clear evidence that testosterone stimulate EPO secretion. For example, administration of graded doses of testosterone to healthy young and older men increased hemoglobin and hematocrit but did not change EPO levels **(Coviello, *et al*., 2008)**. Erythrocytosis in some other testosterone trials also was not associated with increased EPO levels **(Maggio *et al*., 2013)**. Furthermore, testosterone failed to directly activate EPO transcription in Hep 3 B cells, an EPO-screting cell line that is highly sensitive to hypoxia induction **(Blanchard *et al*., 1992)**. Therefore, alternative mechanisms of testosterone-induced erythrocytosis have been suggested including direct effects on bone marrow erythroblasts and on red cell survival **(Shahani *et al*., 2009)**.

Testosterone injection had no significant effect on the values of MCV, MCH, and MCHC. The MCV (mean corpuscular volume) is the average volume of red cells in the blood specimen. The value of MCV in this study was within the normal range (50-75 fl) reported by **Cooke (2000)**. This normal value indicates normocytic cells (normal average RBC size). **Alen (1985)** who studied the hematological and hepatic effects of testosterone self-administration in five power athletes during 26 weeks training also found no change in the value of MCV even though there was an increase in RBC count and hematocrit. **Palacios *et al*. (1983)** reported negligible increase in MCV with mild but significant increase in RBC, hematocrit, and hemoglobin in normal men administered testosterone enanthate. The mean corpuscular hemoglobin (MCH) is the average mass of hemoglobin per red blood cell in a sample of blood, and the mean corpuscular hemoglobin concentration (MCHC), which is a measure of the concentration of hemoglobin in a given volume of packed red blood cells were within the normal range for rabbits. This indicates that hemoglobin production and iron metabolism in the RBC of these rabbits are normal, which means that the increases in HGB and HCT are due to increase in RBC production. However, testosterone treatment in older men with mobility limitation resulted in small decrease in mean corpuscular volume and mean corpuscular hemoglobin concentration **(Bachman *et al*., 2014)**. But **Palacios *et al*. (1983)** noticed negligible increases in MCH and MCHC in normal men administered testosterone enanthate. In Japanese quail chicks, testosterone propionate had no significant effect on MCV, MCH and MCHC even though testosterone administration resulted in an elevated erythrocyte count, hematocrit reading and hemoglobin level **(Nirmalan and Robinson, 1972)**.

The doses of testosterone used in this study had no significant effect on the WBC count when compared with that of the control. **Kamis and Ibrahim (1989)** found that testosterone suppresses the production of leukocytes and that the testosterone-treated mice become more susceptible to parasite infection. **Brand *et al*. (2012)** reported that there was an inverse association between endogenous total testosterone and sex hormone-binding globulins (SHBG) levels and total WBC and granulocytes count in middle aged and older men. But **Palacios *et al*. (1983)** reported a mild but significant increase in white blood cells in normal men administered testosterone enanthate. In Japanese quail chicks, testosterone administration had no significant effect on leucocyte count and percentage of basophils and eosinophils **(Nirmalan and Robinson, 1972)**.

In this study testosterone was found to increase the level of platelets in the blood of treated rabbits. An increase in platelets count in castrated rabbits treated with testosterone undecanoate was also reported by **Zhao *et al*. (2013)**. They suggested that testosterone could enhance the platelet count by stimulating the proliferation of erythroid and myeloid progentors. Platelets play a key role in thrombus formation through adhesion to the vascular wall, aggregation and stimulation of coagulation through release of metabolites such as thromboxane A2 which further promotes platelets activity and vascular muscle contraction. *In vitro* studies in animal models suggest that testosterone deficiency is associated with decreased platelet aggregation and thromboxane A2 receptor density, with testosterone therapy improving platelet activity and thromboxane A2 receptor density **(Matsuda *et al*., 1994)**. In healthy young men testosterone injection was shown to increase platelet aggregation activity and thromboxane receptor density **(Ajayi *et al*. 1995)**. In a study using a human megakaryocytic cell line, administration of testosterone in culture suggested platelet aggregation **(Lee *et al*., 2012)**. In animal studies with rat aortic endothelial cells, testosterone administration in vitro resulted in reduced platelet aggregation **(Cutini *et al*., 2012)**. Thus,

animal and human data suggest a mixed effect of testosterone on platelet activity and function.

It is believed that testosterone exerts its hemopoietic effect, at least partly, by affecting the maintenance of erythroid and granulocytic stem cells, or directly by increasing the input from multipotent stem cell pool, or by both mechanisms **(Beran *et al.*, 1982)**.

It is concluded that the increase in RBC count could result in the thickening of the blood and the increase in hematocrit value could increase the risk factors for abnormal clotting; therefore, the benefits of using testosterone to increase weight and muscle strength must be weighed against the potential risk of cardiovascular disease.

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