Journal of Pharmaceutical Research International

33(51B): 164-169, 2021; Article no.JPRI.77261
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Effect of *Nigella sativa* on Testosterone Level in Albino Rats Treated with Doxorubicin

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i51B33526
Editor(s):
(1) Dr. Dharmesh Chandra Sharma, G. R. Medical College & J. A. Hospital, India.
Reviewers:
(1) Victor Baba Oti, Nasarawa State University, Nigeria.
(2) Waleska dos Santos, Federal University of Sergipe, Brazil.
Complete Peer review History, details of the editor(s), Reviewers and additional Reviewers are available here: https://www.sdiarticle5.com/review-history/77261

Original Research Article

Received 10 September 2021
Accepted 20 November 2021
Published 25 November 2021

ABSTRACT

Objective: To measure the influence of *Nigella sativa* on testosterone level of albino rats treated with doxorubicin
Study Design: Investigational study.
Place of Study: Animal House, JPMC, Karachi,
Materials and Methods: This study was accompanied on 3-4 months old, 40 albino rats, in the animal house of BMSI, Anatomy department, Karachi for 5 weeks were taken for this study and distributed into 4 groups, A1, A2, A3 &A4. A1 served as control, A2 receive Doxorubicin 3 mg/kg /week intraperitonealy, A3 receive extract of *Nigella sativa* 1000mg/kg daily orally along with Doxorubicin 3 mg / kg /week intraperitonealy and A4 receive extract of *Nigella sativa* 1000mg/kg daily orally. At completion of study, animals were sacrifice and tissues were preserved for staining.
Time of Study: The time of study was 35 days.

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Results: In A2 serum Testosterone was markedly decreased, i.e 3.093+0.091 ng/ml as compared to A1 though serum levels were extremely substantial raise in A3 when compared with A2. This shows amended role of *Nigella sativa* on Doxorubicin induced kidney.
Conclusion: This study reveals that *Nigella sativa* amended the serum levels of testosterone of doxorubicin induced kidney.

Keywords: NS(Nigella sativa); TQ (thymoquinone); folkoric; n (number); ng (nanogram).

1. INTRODUCTION

Subsequently to cardiovascular diseases the second leading cause of death is Cancer globally [1]. In 2012 the probable new cases of cancer are 14.1 million while cancer-related deaths take place are about 8.2 million [2].

Cancer management encompass surgical procedure, chemotherapy, radiotherapy, hormonal treatment, immunotherapy and bone marrow replacement [3]. Local procedures of treatment like; surgery and radiation are more successful when cancer cells are not metastasized, however systemic approach (chemotherapy) is required along with local procedures when early signs of micro metastasis are appeared [4]. More than half million Americans receive chemotherapy each year [5]. Doxorubicin is a potent medication widely use in various kinds of cancer but it causes cell injury and germ cell apoptosis [6]. It induces a significant decline in testis weight, sperm count and testosterone level [7,8,9]. Testosterone is liable for secondary masculine feature development and produced by the mitochondria and the smooth endoplasmic reticulum of leydig cells [10,11], 4 -9 mg/d testosterone is present in fully-grown male and in women slight amount of testosterone is produced by ovary and adrenal gland [12,13]. It is the chief androgen that keeps male development. At the onset of puberty testosterone take part in the progressions from a boy to manhood, like development of male sex organs and secondary sexual characters, upsurge of height and weight along with enlargement of Adam's apple. It also involved in maintenance of libido, bone density and sperm production [14].

Nigella sativa is a folkloric blossoming plant of family *Ranunculaceae* naturally present in south west Asia and nurtured in Middle Eastern Mediterranean region, South Europe, Syria, Turkey, Saudi Arabia, Pakistan, India. In Islam it has a great significance as healing plants. Our prophet Muhammad stated that it can heal all diseases excluding death, so it is also present in tibb-e-nabvi [15,16]. *Nigella sativa* seeds are utilized extensively in traditional medicines due to its phytochemical antioxidants antioxidant, anti-inflammatory, antidiabetic and gastroprotective properties [16,17]. Furthermore it was bring into knowledge that its extract has anti-tumor effects which reduces side effects of chemotropic agents as well as improves the seminal fluid properties by reducing free radicals in seminal plasma. In this manner it increases fertility by improving plasma levels of gonadrotopins and testosterone in albino rat [16,17,18]. It is used in numerous therapeutic purposes like in malignancy, dyslipidemia, metabolic syndrome, diabetes, asthma, convulsion, palliative, anti- tussive, anti-inflammatory, and anti-oxidant abilities due to its active constituent TQ (thymoquinone) [19,20,21], Its antimicrobial effects comprises on microbes thus provide support to immune system [21,22]. NS oil improves plasma testosterone level, semen results, testicular biomarkers, steroidogenic enzymes and testicular morphology by quashing lipid peroxidation and free radical overproduction. This happens due to thymoquinone which has a key role in testicular protection due to its antioxidant, anti-apoptotic effects. It is also defensive against upper respiratory diseases, GIT disorders and skin problem [23,24,25].

This research work shows that *nigella sativa* has protective role against doxorubicin nephrotoxicity. In the prevailing time, any new study regarding influence of *nigella sativa* on serum testosterone with effects of doxirubicin on albino rats were not came into notice thus this chance is taken to initiate this work and relate the consequences with prior studies.

2. MATERIAL AND METHODS

This study was accompanied on 3-4 months old, 40 albino rats, in the animal house of BMSI, Anatomy department, Karachi for 5 weeks. All the rats were retained beneath surveillance to evaluate their well-being for 7 days. All albino rats were separated into four clusters, ten animals in each cluster.

A1 = Control.
A2 = Doxorubicin 3 mg/kg /week intraperitonealy.
A3 = extract of *Nigella sativa* 1g/kg daily by mouth along with Doxorubicin 3 mg / kg /week intraperitonealy.
A4 = extract of *Nigella sativa* 1g/kg daily by mouth for 5 weeks.

Animals were saw regularly for their general physical activities and fitness. At the completion of experiment blood samples were taken by direct intra cardiac puncture for revealing of Testosterone level. Samples were retained for clot formation for thirty minutes to one hour. The samples were centrifuged at 1000 cycles /seconds for 30 minutes and the alienated serum was stowed in lab freezer at -20℃ for two hours prior the assessment of testosterone level.

3. ARITHMETICAL INVESTIGATION OF STATISTICS

It was assessed by the paired sample student's test.

The variance was observed statistically substantial. All calculations were done by utilizing computer software SPSS version 20.0.

4. OBSERVATIONS ON TESTOSTERONE LEVEL

4.1 A1

In A1 animals mean value of serum levels of testosterone was 6.663+0.164 ng/ml (Table 1).

4.2 A2

In A2 animals mean value of levels of testosterone was 3.093+0.091 ng/ml (Table 1). There was highly substantial reduction of levels of testosterone **(**p<0.0001) in A2 as compared to A1. (Table 2 & Graph 1).

4.3 A3

In A3 animals mean value of levels of testosterone was 6.178+0.12 ng/ml (Table 1). There was substantial decline in serum levels of testosterone (p< 0.0311) as compared to A1 (Table 2). There was extremely substantial raise of levels of testosterone in A3 **(**p<0.0001) when compared with A2 (Table 2 & Graph 1).

Table 1. Mean serum levels of testosterone in various rat groups

(n=40)	Management received	Post treatment testosterone
A1	Control	6.663±0.164
A2	Doxorubicin	3.093±0.091**
A3	Doxorubicin and *Nigella sativa*	6.178±0.127*
A4	*Nigella sativa*	7.186±0.159**

Quantity of albino rats
Mean±SEM
P<0.05 (*) is statistically substantial
P<0.01 (**) is highly substantial

Table 2. Assessment of mean serum levels of testosterone between numerous rat groups

Sets	T-test	P-value
A1 & A2	17.308	0.0001**
A1 & A3	2.3382	0.0311*
A1 & A4	5.732	0.0001**
A2 & A3	-17.367	0.0001**
A4 & A2	22.0798	0.0001**

P<0.01 (**) is extremely substantial

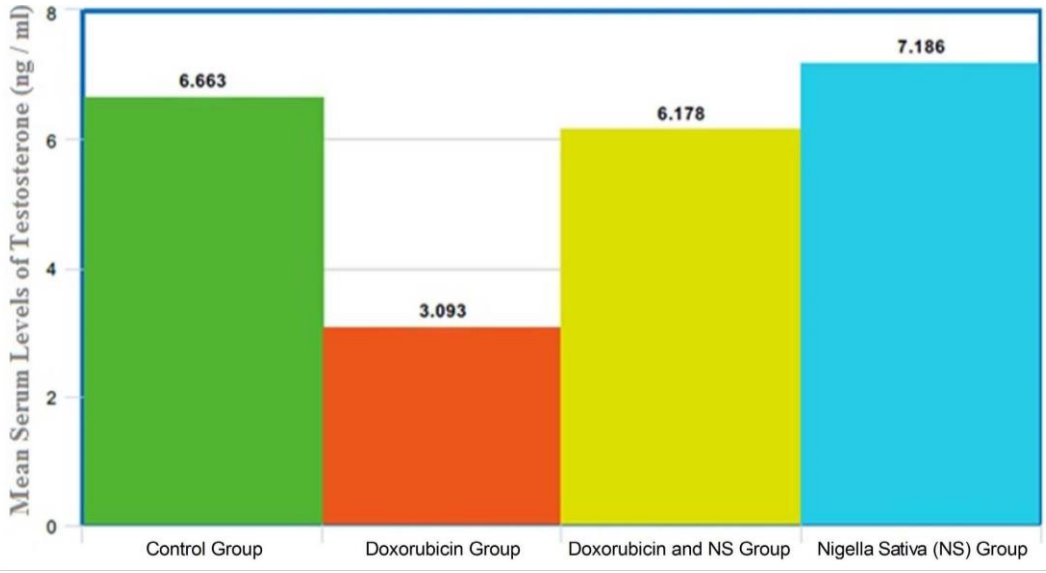
4.4 A4

In A4 animals mean value of serum levels of testosterone was 7.186+0.159 ng/ml (Table 1). There was extremely substantial raise in serum levels of testosterone of A4 **(**p < 0.0001) when compared with A1 (Table 2). The statistics also exhibited extremely substantial raise in serum levels of testosterone in A4 (p < 0.0001) when compared with A3 and A4 respectively (Table 2 & Graph 1).

5. DISCUSSION

Anterior pituitary gland secretes luteinizing LH and it stimulates the testosterone production in Leydig cells, and spermatogenesis [8]. Leydig cells are found in child's testis for a few weeks after birth and then the interstitial Leydig cells become absent. Restitution of Leydig cells constitutes about twenty percent mass in the adult testis and secretes Testosterone which is liable for the growth, stimulation and secretary activities of male genitilia. It is necessary for spermatogenesis and maintenance of secondary sexual features. Disruption in the androgens production had adverse influence on reproduction [13].

A2 animals showed significantly decreased testosterone level as compared to groups A1, A3and A4. This is in agreement with [8] who



Graph 1. Mean serum level of testosterone (ng/ml) in different groups of albino rats

suggested that Doxorubicin causes the generalized toxicity in rat testis due to free radical production with the same dose as per our study. This may be due to depletion of leydig cells by Doxorubicin, which is supported by histopathological findings. Testosterone is prime regulator of spermatogenesis; decreased level of testosterone is supposed to be the cause of infertility [9], who further support our findings with the same dose in male adult wistar rats [10].

Increase in testosterone level in A3 as compared to A2 (doxorubicin treated) might be due to ameliorating effects of *Nigella Sativa* as supported by [11] that *Nigella Sativa* acts as effective free radical scavenger. Solvent extraction of *Nigella Sativa* contains eight unsaturated fatty acids [20,21] and these unsaturated fatty acids provoke the action of 17 β- hydroxysteroid dehydrogenase, which is a key factor in testosterone biosynthesis pathway [18]. This is also supported by [16] that aqueous suspension of *Nigella sativa* increases testosterone level after being administered at the same dose as per our study, in Colchicin injured testes, by distinct retrieval of germinal lining of semniferous tubules and leydig cells [19] is also in agreement that the testosterone level increases after administration of *Nigella sativa*, in Alloxan induced diabetic Wister rats.

There was marked increase in testosterone level in A4 (treated only with *Nigella sativa*) as compared to groups A1, A2 and A3; this is in agreement with findings of [24,25], who reported that 2g of *Nigella sativa* capsules for three months significantly increases the testosterone and other reproductive hormones in humans [23, 24] also support our findings.

6. CONCLUSION

Research determined that A2 animals had reduced level of testosterone but in A3 animals we observe raise level of testosterone as compared to A2. Therefore our assumption from this study is that avoid the usage of Doxirubicin and if mandatory don't use it without nigella extract, in order to decrease its harmful effects.

7. LIMITATION OF STUDY

Funds are not sufficient otherwise we will do it in further depth.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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