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Effects of Zingier Officinale Ethanolic Extract on Some Blood Plasma Parameters in The Wistar Male Rat Treated with Doxorubicin

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ABSTRACT

Background and objectives: *The present study aims to investigate whether Zingier could protect against doxorubicin induced testicular toxicity.*
Materials and Methods: *56 adult Wistar male rats were randomly divided into 6 groups of 8: the control, the sham or experimental group 1 receiving 3 mg/kg.bw DOX, experimental groups 2 and 3 receiving 500 and 1000 mg/kg.bw ginger extract, and Experimental groups 4 and 5 receiving 500 and 1000 mg/kg extract + 3 mg/kg DOX respectively. The extract was orally administered an hour after intraperitoneal injection of doxorubicin. DOX injection was carried out once a week for four weeks. Plasma FSH, LH and testosterone levels were assayed*
Results: *according to the findings DOX treatment decreased the plasma hormones levels FSH, LH and testosterone. Consumption of ethanoic ginger extract and doxorubicin significantly improved the induced toxicity.*
Conclusion: *ginger alcoholic extract can prevent doxorubicin toxic effect on sexual hormonal and improve male reproductive activities.*

Keywords*: Doxorubicin; testicular toxicity; testosterone; ginger*

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INTRODUCTION

In recent years, infertility and its related problems have become an important issue in couple's life (Ebisch et al. 2007) Factors such as toxins, anticancer drugs also adversely affect spermatogenesis and thus, increase the prevalence of infertility (Badia, 2008).
Doxorubicin (DOX) is an anthracycline antibiotic (Lebrecht, D 2007).
Doxorubicin, a known anticancer drug, is an antibiotic produced by the fungus Streptomyces peucetius. Many reports have shown that DOX can Cause long and short term male infertility (Zanetti-2007). In addition, DOX is an intracellular oxidative stress inducer, and can cause biochemical and physiological abnormalities that ultimately culminate in cytotoxicity DOX has intercalation into DNA and disruption of topoisomerase-II-mediated DNA repair and generation of free radicals and their damage to cellular membranes, DNA and proteins (Yeh Y-2007). That has a wide variety of toxic side effects on organs including liver (Patel N. 2010), kidney (Ahmed, R2010), heart (Miyata, S. 2010), brain (Rousselle, C 2001) and testis (Abdella, E 2009).
Medicinal plants have been essential for humans to reduce illnesses from the dawn of civilization (NAYAK et al. 2011).

Ginger (Zingiber officinale) is an edible plant, spice or herb. It belongs to Zingiberacea family and is similar to the orchid(Iwami M-2011)
Components of ginger, including essential oils, zingiberol, zingiberone, zingiberene, and pungent agents such as gingerol and with other gingerol analogues such as the shogaol, paradol and zingerone have been identified (. Hanan F Aly-2013)
The phenol compounds derived from ginger (gingerol and shogaol) have many physiological and pharmacological activities. Although, it has been used for centuries, this plant still attracts extensive search attention (Lin R-2010). Gingerols present in ginger are involve in destroying free radicals and are anti-serotonergic and inhibitors of prostaglandin production (Amin A-2006)

This work was performed to show the action of Z. Officinale extract on reproductive functions and antioxidant activities in male rats treated with doxorubicin.

MATERIALS AND METHODS

56 adult male Wistar rats weighing approximately 240 ± 10 g and about 3-4 months old used in this study were kept in standard laboratory conditions in Kazerun Islamic Azad University animal house. The animals were housed in clear polypropylene cages lined with wood chip beddings. They were fed with standard pellet diet and water was made available at all times. prepare ginger alcoholic extract, percolation method was performed. The extract was gavaged orally from the first day an hour after doxorubicin (Ebewepharma companies) injection for four weeks. DOX was administered intraperitoneally once a week at the concentration of 3mg/kg.bw (Zanetti SR-2007). 56 adult Wistar male rats were randomly divided into 6 groups of 8: the control, the sham or experimental group 1 receiving 3 mg/kg.bw DOX, experimental groups 2 and 3 receiving 500 and 1000 mg/kg.bw ginger extract, and Experimental groups 4 and 5 receiving 500 and 1000 mg/kg extract + 3 mg/kg DOX respectively. All

experimental procedures were done according to the guidelines of Animal Ethical Committee of National Research Center (Abdel-Aal-2013).
At the end of the treatment period, animals were ethically anesthetized by ether,Blood samples were spun at 2500rpm for 15 minutes in a table top centrifuge. The serum samples obtained were analyzed to determine the
concentration of testosterone , LH, FSH. The analysis was carried via the tube-based enzyme immunoassay (EIA) method. The protocol used for the hormone
was according to the method described for the kit (Immunometrics Limited UK) and meet the WHO standards in research programme for human reproduction.

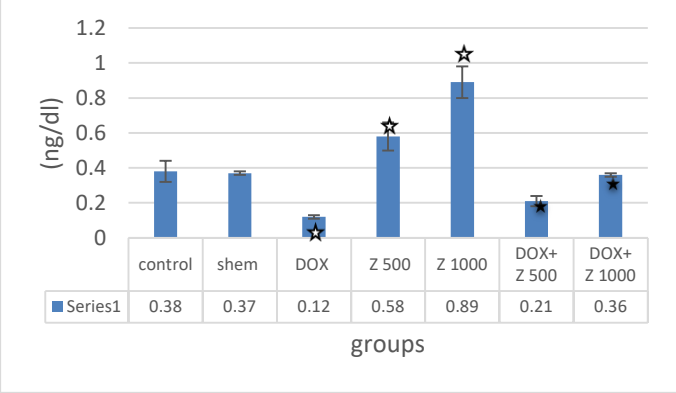
Statistical analysis

Data were analyzed using SPSS statistical package (Version 17.0, SPSS Inc., Chicago IL, USA) for Windows. ANOVA test was used to determine the differences between the groups. The level of statistical significance was set at $p < 0.05$.

RESULT

Table 1 shows the changes in the serum testosterone levels of different groups receiving ginger extract(group 2,3) There were dose and duration dependent increases in the serum testosterone levels in the Z. Officinale administered rats compared with the controls and shem .
The levels of testosterone in the DOX group compared to the control group showed significant decrease, while significant increase was observed in experimental groups 500, 1000 mg/kg extract + 3 mg/kg DOX relative to experimental DOX group. (table. 1).
table 2 shows the changes in the serum LH and FSH levels of different groups receiving ginger extract(group 2,3 dose dependent increases in the serum LH and FSH levels in the Z. Officinale administered rats compared with the controls and shem .
Moreover, administration of DOX significantly reduced level of LH and FSH are compared to the untreated control group. However, the level of LH and FSH were significantly increased in the experimental group's 500, 1000 mg/kg extract + 3 mg/kg DOX relative to the experimental group DOX (Table 2). ($P<0.05$).

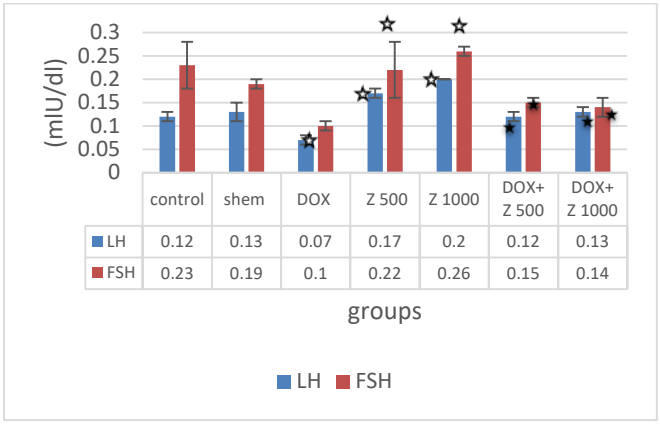
Table 1: Effects of Z. Officinale and DOX on testosterone level after treatment.



★ There are Significant differences between the experimental group compared with their control and shem group. ($P \leq 0.05$).

★ There are Significant differences between the experimental group compared with their experimental group1 (DOX) ($P \leq 0.05$).

Table 2: Effects of Z. Officinale and DOX on LH and FSH level after treatment.



☆ There are Significant differences between the experimental group compared with their control and shem group. ($P \leq 0.05$).

★ There are Significant differences between the experimental group compared with their experimental group 1 (DOX)($P \leq 0.05$).

DISCUSSION

DOX can Cause long and short term male infertility (Zanetti-2007).. The results of the present study suggested that Zingiber Officinale have a eneficial effect on male reproductive functions in rats.

studies shows that attributed the effect of doxorubicin on reproductive performance to the destruction of meiotic and early spermatogenic stages (Miyata, S-2010) so Manabe et al. (Manabe F-1997) showed that interperitonal injection of DOX induces testicular weight loss, tubular atrophy and sharp decline in the number of sexual cells in rat. it has been shown that in addition to impairing spermatogenesis and reducing sperm count, DOX can increase oxidative stress and reduce antioxidant activity as well (Yeh Y-2007)

Testosterone is known to be critically involved in the development of sperm

cells and derangement results widely in leydig cell dysfunction and testicular steroidogenic disorder (Zhang et al, 2001).

In the present study, use of DOX significantly reduced , testosterone, LH, FSH

levels (table 1-2) this finding is in agreement with other reports indicating that anti-cancer drugs can adversely affect Leydig cells leading to a reduction in number as well as abnormal maturity (Brilhante O-2011). In consistence with our findings, it has been reported that animals treated with a single dose of doxorubicin showed low serum levels of free testosterone compared with the control group (Abdella, E 2009). in our study the treatment of these rats with DOX +ginger induced an increase of the testosterone, LH, FSH levels .

In traditional medicine, ginger is used in the treatment of various diseases such as rheumatism, fever, dementia, hypertension, vomiting, constipation, pain, infection, asthma, diabetes, ETC. Apparently, it is anti-apoptotic, powerful antioxidant (to prevent free radical production), anti-inflammatory and sexual enhancer (Rehman R-2011)

The ginger contains phenol compounds (gingerol and shogaol) have many physiological and pharmacological effect. (Lin R-2010) Studies suggested that extract of Zingiber Officinale possesses pro-fertility properties in male rats which can be a product a potent of antioxidant and androgenic activities (Morakinyo A-2008). our observation show that zingiber increased, testosterone, LH, FSH levels in the experimental groups 500, 1000 mg/kg extract + 3 mg/kg DOX compaire to experimental group DOX.

CONCLUSION

Fertility disorders are clinically important following chemotherapy. In conclusion, zingiber has antioxidant properties and androgenic activities so treatment with zingiber may protect the testis from testicular dysfunction caused by doxorubicin.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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