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The effect of royal jelly on some biochemical parameters on male albino rats treated Nitrofurantoin

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Nitrofurantoin, a safe antimicrobial drug as per literature is found to be the most effective therapeutic option for treating uncomplicated UTI even in multidrug resistant Uropathogenic Escherichia Coli (UPEC).Rats were randomly divided into four groups,group2 is treated with royal jelly(RJ) ,group3 treated with nitrofurantoin , group4 treated with nitrofurantoin and RJ.In RJ group the sperm count , sperm viability, sperm motility , FSH ,LH, testosterone increase significantly but sperm abnormal is decrease significantly while in nitrofurantoin group there are decrease significantly in sperm count , sperm viability , sperm motility and MDA but sperm abnormal , FSH, LH ,testosterone, CAT and SOA are increased. RJ may be used in decrease the role injury for nitrofurantion on eperm characteristic ,hormone sex levels and antioxidant enzyme levels.

Keywords: Nitrofurantoin , royal jelly, FSH, testosteron

INTRODUCTION

Nitrofurantoin

Nitrofurantoin is a broad-spectrum bactericidal antibiotic. Since its discovery in 1952, and its use for more than four decades no clinically significant resistance has developed, as seen with other commonly used antibiotics. This is probably because Nitrofurantoin has multiple sites and levels of action in contrast to antibiotics that attack a single target like ampicillin or two targets like cotrimoxazole. A bacterial nitroreductase enzyme converts nitrofurantoin to highly reactive electrophilic intermediates which non-specifically attack bacterial ribosomal proteins, resulting in complete inhibition of protein synthesis (McOsker et al., 1994) and cause single-strand breaks in DNA (McCalla et al., 1970).

Urinary Tract Infection (UTI), one of the major health problems in India, especially for females, is predominantly caused by Escherichia coli. Nitrofurantoin, a safe antimicrobial drug as per literature is found to be the most effective therapeutic option for treating uncomplicated UTI even in multidrug resistant Uropathogenic Escherichia Coli (UPEC). Thus, the use of nitrofurantoin in UTI may be advocated as an empirical drug even in the era of super bugs in our institution as revealed in this current study. Similar studies should be continued to institute proper empirical therapy of the patients, because of the ever changing sensitivity pattern (Konar et al. , 2016). Nitrofurantoin has been available for the treatment of UTIs since 1953. Its current uses include the treatment of uncomplicated UTIs and prophylaxis against UTIs in people prone to recurrent UTIs. (Gary J., 2008) The drug works by causing damage to the bacterial DNA, since its

reduced form is highly reactive. This is made possible by the rapid reduction of nitrofurantoin inside the bacterial cell by flavo proteins (Nitrofuran reductase) to multiple reactive intermediates that attack ribosomal proteins, DNA, enzymes involved in respiration and pyruvate metabolism within the cell. Nitrofurantoin exerts greater effects on bacterial cells than mammalian cells as the former activate the drug more rapidly. Multiple mechanisms of action may likely be responsible for the low development of resistance against this drug. (Tu and McCalla, 1975).

Royal jelly

Royal jelly (RJ) is a pretentious secretion of the hypopharyngeal and mandibular glands of nurse honey bees, which is fed to the queen and younger larvae. RJ performs numerous functions and has been widely used in commercial, medical products, health foods, and cosmetics in many countries around the world (Ramadana and Al-Ghamdi 2012).

MATERIALS AND METHODS

Capsulated pure RJ was provided by Natural Life (Brookvale, NSW, Australia). According to manufacturer's reports, the RJ was produced from the purest beehives which were free from chemicals or antibiotic sprays. To prepare a stock solution of RJ, the contents of each capsule (1,000 mg) were dissolved in10mL deionized water (W/V) to obtain a concentration of100 mg of RJ/mL [Abd-Allah 2012b]. The RJ was added to the deionized water and mixed thoroughly in a shaker at 4_C overnight. The prepared mixture was sterilized using a0. 22 mm filter and stored at _20_C.

Experimental design:

Used for this study were Twenty four adult albino male rats of 8-10 weeks old weighting (245± 5 gm). Rats were randomly divided into four groups, each of six rats as follows: Group 1: Control group, healthy control rats received 0.3 ml isotonic saline solution intra peritoneally (negative control). Group 2: royal jelly(RJ) treated With 100 mg/kg body weight RJ, Group 3: group3 treated with nitrofurantoin , group4 treated with nitrofurantoin and RJ. Rats were given standard diet and tap water *ad libitum*. The experiment lasted for 35 days starting from RJ and nitrofurantoin administration. At the end of the experimental period, rats were deprived of food overnight and sacrificed under ether anesthesia. Blood samples were collected by heart puncture with a fine needle . Collected blood was stored for 30 min at room temperature and centrifuged with 3000 rpm for 15 min. The supernatant kept in - 20 ºC until use. At the end of treatment period, fertility parameters such as sperm motility, viability, abnormality and count, blood testosterone, FSH and LH levels and antioxidant enzyme levels were measured.

Collection and sperms parameters

Rats were killed and dissected directly,the testes were removed and placed in a sterile disposable Petri dish containing 3ml RPMI-1640 medium at 37 ºC, the sperms were collected from the epididymis of rats by the caudal was cut and placed in a Petri dish containing 1ml of RPMI-1640 medium and minced by using microsurgical scissor and forces [Bearden and Faquay, 1992].

Sperm motility

Sperm motility was assessed according to the method reported by [Bearden and Faquay, 1992] Fifty µl of the sperm suspension was placed over a slide and covered by a cover slide. Using light microscope, several fields were examined to estimate the percentage of individual motility of sperms.

Sperm viability and abnormalities

The percentages of dead and abnormal sperms were measured as following according to the method reported by [Bancroft and Steven, 1982]. A drop of the sperm suspension was placed over the slide and, then a drop of Eosin-Nigrosin stain was added and mixed. The mixture was spread using another slide and left to dry. Using light microscope, 200 sperms were counted to calculate the percentages of dead and abnormal sperm.

Biochemical analysis:

At experimental final the blood collection from all animals after were sacrificed blood collected by cardiac puncture via using disposable insulin syringes Samples were put into Eppendorf tubes. Serum was Separated by centrifugation at a speed of 3000 rpm for 10 minutes. A hormone level was estimated by using a sandwich immune detection method as described by.I-CHROMA TM, FSH is according to immunoassay system by antigen antibody interaction and fluorescence technology[Goldstein and Kosasa ,1975] [kim et al., ,2011]. The level of testosterone was measured according to [Frite etai, 2008] through

of method solid phase enzyme –linked immune sorbent assay (ELISA) [D'souza et al.,2012]

RESULTS

Table-1 effect the royal jelly on sperm characteristic of male mice treated with Nitrofurantoin

Group	**Sperm count (X10^6\ml)**	**Sperm viability(%)**	**Sperm motility(%)**	**Sperm abnormality(%)**
control	39.36±3.23 a	90.5 8±3.18a	90.14±2.06 a	10.1 2±1.5 7b
Royal jelly	45.7 0±4.53 b	92.27 ± 2.83a	95.33±5.21a	7.7 5 ±1.18a
Nitrofurantoin	22.11 ±1.8 0c	65.49± 1.23b	60.43±4.50 b	23.1 3± 2.62d
Royal jelly+ Nitrofurantoin	35.34 ±1.3 d	76.40 ±3.03 c	74.33±2.65c	16.23 ±3.21 c

Data are presented as mean S.E.
Different litter refer to the significant difference at ($p<0.05$)

Table-2 Effect of the royal jelly on hormone levels of male mice treated with Nitrofurantoin

group	FSH(mIU\ml)	LH(mIU\ml)	Testosterone(ng\ml)
control	2.21± 0.05a	1.75± 0.05a	3.40± 0.33a
Royal jelly	2.57 ±0.03a	1.79± 0.04a	4.90±0.22b
Nitrofurantoin	1.02 ±0.02b	1.68±0.04a	2.43 ±0.12c
Royal jelly+ Nitrofurantoin	2.09± 0.05a	1.62± 0.02a	4.08± 0.42a

Data are presented as mean S.E.
Different litter refer to significant difference at $p<0.05$

Table-3 Effect of the royal jelly on antioxidant enzyme levels of male mice treated with Nitrofurantoin

Group	MDA(U/ml)	CAT (U/ml)	SOD(U/ml)
Control	1.08± 0.09a	0.6 5±0.05a	1.05± 0.43a
Royal jelly	1.20± 0.22a	0.6 8±0.07a	1.68± 0.54a
Nitrofurantoin	3.80± 0.14b	0.27 ±0.06c	2.42± 0.18b
Royal jelly+ Nitrofurantoin	1.43 0.0 4a	0.19 ±0.01b	1.53 ±0.32b

Data are presented as mean S.E.
Different litter refer to significant difference at $p<0.05$

DISCUSSION

Effect the royal jelly on sperm characteristic of male mice treated with Nitrofurantoin

The Date are shown in the Table -1- there are significant increase in sperm count ,sperm viability , and sperm percentage in treatment group comparative with control group while sperm abnormality percentage was significant decrease. These finding are similar to finding Nawar et al., (2015) so on other band Al-Dujaily etal.(2015).The mice treated with Nitrofurantoin showed decrease in sperm function parameters as sperm count ,sperm viability and sperm motility, while abnormal sperm was increasing .Nitrofurantoin can cause mitochondria dysfunction from through inhibition of these complex (Omidi et al.,2016).

In one study, observed effect of nitrofurantoinon male mice reproductive system and testicular tissue (Al-Azawi and Asker, 2017). There for using Royal jelly with nitrofurantoin leased from the negative effect of nitrofurantoin drug on sperm

function parameters.

Effect the royal jelly on hormone levels of male mice treated with Nitrofurantoin

In this study The Table -2- shown there is no significant increase in FSH, LH levels in Royal jelly group treated, but there is a significant increase in testosterone level. Either nitrofurantoin drug group there are significant decreases in FSH and Testosterone levels, but LH was no significant. While Royal jelly and nitrofurantoin where are no significant decrease about the control group. Royal jelly may be used in decreased of inhibited effect for nitrofurantoin from through sex hormonal profile increased by used RJ ,in one study , RJ acted on increase the levels or FSH ,LH and testosteron hormone and also caused lowered DNA damage (yong et al.,2012; Zahmatkesh et al.,2014).

Effect the royal jelly on antioxidant enzyme levels of male mice treated with Nitrofurantoin

The date in table -3- showed there are no significant increase in MDA, CAT and SOD enzyme level in Royal jelly group. Royal jelly used as natural antioxidant for protect the tissues from damage that courses by free radical (khannm et al., 2004). royal jelly has a high ability to elimination a free radical and lowering the toxicity for chemical agents, In other study royal jelly determined were activities Malondialdehyde(MDA) and Superoxide dimatase (SOD) (Alvarez-Suarez ,2017).For role in lower in biochemical parameters (SOD , CAT and MDA) So decrease in oxidative stress becouse of royal jelly increased antioxidant activities (Abd El-Monem,2011).

CONCLUSION

In conclusion, we have demonstrated that Nitrofurantoin may result in the failure of normal sperm characteristic but with royal jelly reduce the side effect of the drug. As these qualities improve. On the other hand, RJ act on increase in hormone levels as FSH, LH and testosterone that inhibited by nitrofurantoin, also, RJ. act on increase the antioxidant enzyme MDA,CAS and SOD that decrease because of nitrofurantoin drug.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

SMM provided animal house and animal husbandry. MHN performed the experiments and wrote the manuscript and LAS designed experiments, performed data analysis and reviewed the manuscript. All authors read and approved the final version.

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