Effect of Royal jelly and Date Palm Pollen Suspension on Fertility in Adult Male Rats Exposed to Sodium Valproate

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تأثير معلق غذاء ملكات النحل و حبوب لقاح النخيل على الخصوبة في ذكور الفئران البالغة المعرضة لفالبروات الصوديوم

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المستخلص العربي

فالبروات الصوديوم هو دواء واسع الانتشار مضاد للصرع يستخدم بشكل عام لمعظم حالات الصرع مجهول السبب والأعراض. تهدف هذه الدراسة إلى تقييم تأثير غذاء ملكات النحل وحبوب لقاح النخيل ضد السمية في الخصية التي يسببها فالبروات الصوديوم في ذكور الجرذان . تم تقسيم عدد ثلاثين من ذكور الجرذان البيضاء إلى خمس مجموعات.المجموعة الأولي ، (المجموعة الضابطة السالبة) ، بينما تلقت المجموعات الأربعة الأخرى فالبروات الصوديوم (٥٠٠ مجم / كجم / يوم) لمدة أسبوع ثم قسمت الي : المجموعة الثانية كمجموعة ضابطه إيجابية ،المجموعة الثالثة تعطى سيترات السيلدينافيل (الفياجرا ٥ مجم / كجم) عبر أنبوب معدة يومياً في صورة معلق مائي على التوالي لمدة ٢٨ يوم. ،تلقت المجموعة الرابعة جرعات يومية من حبوب لقاح النخيل عبر أنبوب معدة يومياً في صورة معلق مائي (٢٤٠ مجم / كجم).المجموعة الخامسة تلقت جرعات يومية من غذاء ملكات النحل عبر أنبوب معدة يومياً في صورة معلق مائي (٢٠٠ مجم / كجم غذاء).في نهاية فترة العلاج (٢٨ يومًا) ، تم ذبح الفئران ، وتسجيل أوزان الأعضاء الجنسية وعدد وخصائص الحيوانات المنوية ، ومستويات الإنزيمات المضاده للأكسدة و MDA، ومستوي الهرمونات الجنسية (التستوستيرون ، والهرمون المنبه للحويصله , الهرمون الملوتن).أظهرت النتائج أن العلاجات التجريبية قد حسنت من وظائف الكبد ونشاط الحيوانات المنوية ونشاط إنزيم مضادات الأكسدة ومستويات هرمون التستوستيرون ، لذلك فإن تناول غذاء ملكات النحل وحبوب لقاح النخيل قد يكون مفيدًا لتحسين الأداء الجنسي للذكور.

الكلمات المفتاحية: الهرمون الملوتن ، الديسموتاز الفائق ، الإنزيم المضاد للأكسدة ، وظائف الكبد.

Effect of Royal jelly and Date Palm Pollen Suspension on Fertility in Adult Male Rats Exposed to Sodium Valproate

Abstract:

Valproate (VPA) is a wide range antiepileptic drug (AED) used by most idiopathic and symptomatic generalized epilepsy as a first-line agent. In humans, it has been demonstrated that valproate induce endocrine disorders in both sexes. This study was intended to evaluate the effect of royal jelly and date palm pollen (DPP) against testicular toxicity induced by sodium valproate in male rats. Thirty mature male albino rats were divided into five groups of sex rats. **Group(1),** as negative control group, whereas the other four groups received sodium valproate (500mg/ kg / day) for one week and divided into submain groups: **group (2)** as positive control group, **group (3)** given sildenafil citrate (5 mg/kg) via a stomach tube daily respectively for 28 days, **group (4)** received daily gavages of aqueous suspensions date palm pollen by stomach tube (240 mg/kg) and **group (5)** received daily gavages of aqueous suspensions royal jelly by stomach tube (200 mg/kg. diet) . At the end of the treatment period (28 days), rats were sacrificed, weights of sexual organ recorded and their sperm characteristics count, antioxidant enzyme factors levels (catalase , superoxide dismutase) and malondialdehyde were assessed in testicular tissue .Serum sex hormone levels (testosterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) and liver function were analyzed. Histopathological examination was done for the left testis. Results showed that the experimental treatments improved liver function, sperm parameters, antioxidant enzyme activity and testosterone hormone levels, Therefore, the administration of royal jelly and date palm pollen may be beneficial for improving male sexual performance.

Keywords: luteinizing hormone, superoxide dismutase, antioxidant enzyme, liver function.

Introduction:

Epilepsy is one of the most prevalent progressive brain diseases of the cen-tral nervous system. Antiepileptic drug (AED) therapy is the first-line treatment for epilepsy, and approximately 60 percent-70 percent of epilepsy patients can regain seizure control through medicine. Valproate (VPA) is a common antiepileptic drug, which is important against many kinds of convulsions **(Zhao *et al.*, 2018)**. In the treatment of primary generalized seizures, tonic-clonic seizures, myoclonic seizures and absence seizures, it is considered to be highly successful. Several reproductive factors may interact with VPA, which could lead to sexual and reproductive dysfunction in male epilepsy patients. Also it has been reported that VPA is associated with decreased sperm motility and increased morphologically irregular sperm volume, as well as low testicular size in epileptic males **(Zhao *et al.*, 2018)**. The causes of male reproductive toxicity and spermatogenesis of VPA were credited to cytotoxic effect on the testis leading to decrease in serum testosterone, FSH and LH levels **(Bairy *et al.*, 2010).**

The hypopharyngeal glands of honeybee's secreted creamy material called royal jelly (RJ), its constituents contain lipids (fatty acids and sterols), glucose, protein, minerals and vitamins. RJ has a range of useful properties, including antineoplastic, antioxidant, anti-inflammatory, anti-allergic, hypotensive and immune-stimulating. In addition, more studies have shown that RJ has positive potential for male reproductive organs and reproduction in addition to its function against mediated oxidative testicular disease **(Tohamy *et al.*, 2019).**

Date palm pollen (DPP) from ancient times, male palm germ powder, flowers) are used as a dietary supplement to enhance reproductive efficiency in men and women.

DPP has a high nutritious value because it is abundant in phytochemicals such as alpha-amirin, estrone, triterpenoidal saponins flavonoids, estrone, estradiol, estriol, and a crude gonadotrophic material. DPP is also a rich source of natural antioxidants as well **(El-Sisy *et al.*, 2018).** Therefore this research was carried out to determine the toxic effect of valproate for male reproductive organs and fertility

and the possible protective function of RJ and DPP in reducing the harmful effects of valproate in albino rats.

Material and methods:

Chemical and reagents

-Sodium valproate (Depakin) (200 mg/ml) is a product of the Paris, France, Sanofi-Synthelabo Company.

- Crude royal jelly and date palm pollen were purchased from Harraz market, Egypt.

- Cellulose, vitamins, minerals, choline chloride and neutral casein, were be obtained from El-Gomhoriya, Company for Trading Drugs, Chemicals and Medical Instruments, Cairo, Egypt. Corn starch was obtained from local market, Tanta, Egypt.

Experimental design:

Thirty mature male rats of *Sprague Dawley strain* (12-week old, weighing 160 ±10 g) which were obtained from the Laboratory Animal Colony, Helwan, Egypt. They were raised in plastic cages, fed basal diet, and allowed feed and water *ad libitum*. Rats were randomly allocated into groups: **Group (1)** fed on basal diet according to **Reeves *et al.*, (1993)** and kept as negative control group and received saline. Rats of the other four groups were given sodium valproate in a dose of (500 mg/kg b.wt. / day) for a week to induce testicular damage according to **Hamza and Amin, (2007).** After one week they divided into: **Group (2)** fed on basal diet and kept as positive control group. **Group (3)** fed on basal diet and given standard drug (sildenafil citrate) (Viagra, 5 mg/kg) via a stomach tube daily for 28 days according to **(Ahmed and Aslam , 2018). Group (4)** fed on basal diet and received daily gavages of aqueous suspensions date palm pollen by stomach tube (240 mg/kg) for 28 days according to **(Mehraban *et al.*, 2014).Group (5)** fed on basal diet and received daily gavages of aqueous suspensions royal jelly by stomach tube (200 mg/kg. diet), for 28 days according to **(Ebadimanas, 2018).**At the end of experiment, all rats were fasted overnight and sacrificed the blood sample collected and centrifuged to obtain the serum. Seminal vesicles and prostate glands were collected. The testes were removed, cleaned in saline solution, dried by filter paper and weighed. The right testis rapidly taken on ice bags and frozen at – 18°C for assessment of lipid

peroxidation and antioxidant activity in testicular tissue. The left testis were kept in formalin solution (10%), according to the method described by **Drury and Wallington (1980)** for histological examination.

Biological evaluation:

During the experiment (28 days), feed intake was recorded everyday (feed intake), and body weight was recorded every week. Biological evaluation of the different diets was carried out by determination of body weight gain % (BWG %) feed efficiency ratio (FER) according to **Chapman *et al.*, (1959).**

Biochemical analysis of serum:

Determination of serum creatinine described by **Faulkner and King (1976),** serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined according to **Bergmeyer *et al.*, (1986).** Serum luteinizing hormone was carried out according to **Loraine and Bell, (1976),** serum follicle stimulating hormone was carried out according to **McCann and Kirkish, (1985)** and serum testosterone hormone was carried out according to **Hong and Hay Yuen, (2003).**

Assessment of oxidant/antioxidant activity in testes tissue including:

Superoxide dismutase (SOD) according to **Kono, (1978),** Catalase according to **Aebi, (1984)** and malondialdehyde (MDA**)** according to **Placer *et al.*, (1966).**

Semen analysis:

The semen samples were obtained by cutting of cauda epididymis using razor blades and squeezed into clean watch glass. The obtained semen content was diluted 10 times with 2.9% sodium citrate solution and rapidly examined to estimate sperm cell count the percentage of sperm progressive and motility as described by **(Bearden and Fluquary, 1980).** Thereafter, one drop of semen suspension withdrawn, smeared on a glass slide stained by Nigrosin and Eosin (N&E) stain and examined microscopically to determine sperm vitality (alive/dead ratio).

Histopathological examination:

The left testis was fixed in 10% neutral buffered formaldehyde solution at pH 7.5 and cleared in xylol and embedded in paraffin. 4-5 µm thick section prepared and stained with Hematoxylin and Eosin (H&E) for

subsequent histopathological examination according to **Bancroft *et al*, (1996).**

Statistical analysis:

All the obtained data was statistically analyzed by SPSS computer software. The calculated occurred by analysis of variance ANOVA by SPSS.

Results:

The effect of date palm pollen and royal jelly on biological evaluation of rats with testicular injury induced by sodium valproate.

Data present in table (1) showed the effect of injection sodium valproate, date palm pollen and royal jelly on weight gain, feed intake and feed efficiency ratio. The results showed that there were a significant decrease in weight gain, feed intake and feed efficiency ratio in valproate treated group (group 2) compared with negative group (group 1), royal jelly (RJ), date palm pollen (DPP) and viagra groups showed a significant increase in all above parameters compared with positive group ($p<0.05$). Group (5) showed the best result compared with group (1).

Table (1): The effect of date palm pollen and royal jelly on feed intake, body weight gain and feed efficiency ratio of rats with testicular injury induced by sodium valproate

Groups	FI(g/28days)	BWG%	Feed efficiency ratio
	Mean ± SD	Mean ± SD	Mean ± SD
Group (1)	640.00±8.94^{a}	36.43±8.34^{a}	.106±.0186^{a}
Group (2)	450.00±8.94^{e}	5.843 ±3.56^{d}	.035±.004^{d}
Group (3)	555.00±4.47^{d}	19.20±2.57^{c}	.066±.005^{c}
Group (4)	590.00 ±8.94^{c}	26.10±3.49^{b}	.083±.005^{b}
Group (5)	610.00±8.94^{b}	30.20±1.93^{b}	.083±.005^{b}

-Data are presented as mean±SD. Values with different letters indicate significant differences among groups at $p\leq0.05$.

The effect of date palm pollen and royal jelly on weights of male sex organs of rats with testicular injury induced by sodium valproate.

Table (2) showed that the mean ± SD of seminal vesicle weight in the negative control group was 1.80±.104, while seminal vesicle weight in the positive control group was 1.24±.102. Statistical analysis showed significant decrease in seminal vesicle weight for the positive control group compared with the negative control group. Groups (3,4,5) have significant increase values in seminal vesicle weight compared with (group 2).

The results in the table 2 indicated that prostate weight and testes weight recorded significant decrease in positive control group compared with negative group. The other groups showed significant improvement in Prostate weight while there were no significant increases of tests weight of the other different groups compared with positive group.

Table (2): The effect of date palm pollen and royal jelly on weights of male sex organs of rats with testicular injury induced by sodium valproate

Groups	Vesicle weight (g/100 g b.wt.)	Prostate weight (g/100 g b.wt.)	Testes weight (g/100 g b.wt.)
	Mean ± SD	Mean ± SD	Mean ± SD
Group (1)	1.80±.104^{a}	.61±.054^{cb}	5.36±.17^{a}
Group (2)	1.24±.102^{d}	.33±.058^{d}	3.88±.23^{b}
Group (3)	1.41±.103^{c}	.55±.037^{c}	4.16±.52^{b}
Group (4)	1.56±.087^{b}	.62±.050^{b}	4.33±.38^{b}
Group (5)	1.72±.052^{a}	.70±.066^{a}	4.33±.48^{b}

-Data are presented as mean±SD. Values with different letters indicate significant differences among groups at $p \leq 0.05$.

The effect of date palm pollen and royal jelly on testes hermon's (FSH, LH and testesteron) of rats with testicular injury induced by sodium valproate.

Data recorded in table (3) illustrated that sodium valproate caused a significant decrease in (FSH, LH and testesteron) hormones in valproate treated group (group 2) compared with normal rats (group 1). The other treated groups showed significant increase in (FSH, LH and testesteron) hormones compared with positive control group. The best result in tests hermon's were the rats treated with royal jelly.

Table (3): The effect of date palm pollen and royal jelly on testes Hermon's of rats with testicular injury induced by sodium valproate

Groups	FSH (ng/ml)	LH (ng/ml)	Testosterone H. (ng/ml)
	Mean ± SD	Mean ± SD	Mean ± SD
Group (1)	1.28 ±.147[a]	1.65 ±.187[a]	3.35 ±.187[a]
Group (2)	.100 ±.000[d]	.23 ±.021[e]	1.05 ±.122[d]
Group (3)	.78 ±.116[c]	.85 ±.054[d]	2.51 ±.271[c]
Group (4)	.96 ±.196[b]	1.18 ±.075[c]	2.63 ±.121[cb]
Group (5)	1.00 ±.154[b]	1.35 ±.187[b]	2.80 ±.109[b]

-Data are presented as mean±SD. Values with different letters indicate significant differences among groups at p≤0.05.

The effect of date palm pollen and royal jelly on sperm parameters of rats with testicular injury induced by sodium valproate

The results in table (4) indicated that, there were significant decrease in sperm count, sperm motility and sperm viability in group (2) treated with sodium valproate compared with negative control group .Viagra, date palm pollen and royal jelly groups showed significant increase in sperm count, sperm motility and sperm viability compared with positive group. The best result recorded by royal jelly (group 5) followed by date palm pollen group. Sperm abnormality showed a significant increase in group (2) treated with sodium valproate as compared to negative group. All treated groups showed significant decreases in sperm abnormality compared with positive control group.

Table (4): The effect of date palm pollen and royal jelly on sperm parameters of rats with testicular injury induced by sodium valproate

Groups	Sperm count (×10 ^{6} /ml	Sperm Motility (%)	Sperm Viability (%)	Sperm Abnormality (%)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Group (1)	74.16±2.48[a]	88.66 ±1.21[a]	85.83±1.47[a]	1.40±.14[e]
Group (2)	43.33 ± 2.16[e]	59.83 ±1.17[e]	45.00 ±.894[e]	10.50 ±1.05[a]
Group (3)	59.16 ±.752[d]	67.66 ±1.50[d]	54.16 ±1.47[d]	6.50 ±1.05[b]
Group (4)	62.50 ±1.87[c]	71.16 ±1.17[c]	63.00±1.78[c]	5.16 ±.75[c]
Group (5)	66.00 ±1.55[b]	74.16 ±.75[b]	71.33 ±1.21[b]	4.0 0±.89[d]

-Data are presented as mean±SD. Values with different letters indicate significant differences among groups at p≤0.05.

5- **The effect of date palm pollen and royal jelly on antioxidant enzymes and malondialdehyde in testicular tissue of rats with testicular injury induced by sodium valproate.**

Statistical analysis of table (5) showed highly significant decrease in antioxidant enzymes (SOD and CAT) in testicular tissue of the control positive group compared with the negative control group. Viagra, date palm pollen and royal jelly treated groups showed significant increases in antioxidant enzymes compared with positive control group.

Malondialdehyde showed a significant increase in positive control group compared with negative control group. There were significant decreases in other treated groups as compared to positive group (table 5).

Table (5): The effect of date palm pollen and royal jelly on antioxidant enzymes and malondialdehyde in testicular tissue of rats with testicular damage induced by sodium valproate

Groups	SOD (U/min/mg protein)	CAT (U/min/mg protein)	MDA (nmol/mg protein)
	Mean ± SD	Mean ± SD	Mean ± SD
Group (1)	.30±.013^{a}	.29±.015^{a}	.11±.012^{e}
Group (2)	.07±.008^{e}	.12±.017^{d}	.38±.014^{a}
Group (3)	.17±.010^{d}	.18±.008^{c}	.25±.012^{b}
Group (4)	.22±.010^{c}	.19±.008^{c}	.18±.005^{c}
Group (5)	.27±.010^{b}	.27±.008^{b}	.15±.020^{d}

-Data are presented as mean±SD. Values with different letters indicate significant differences among groups at $p \leq 0.05$.

The effect of date palm pollen and royal jelly on liver enzymes and creatinine of rats with testicular injury induced by sodium valproate.

The results in table (6) indicated that there was a significant increase in both AST and ALT in valproate treated group compared with healthy rats (65.50±2.88 and 51.83±1.94 IU/L) and (53.50±2.88 and 35.83±3.18 IU/L), respectively. RJ, DPP and viagra treated groups showed significant decreases in AST and ALT compared with group 2 (positive control group). The mean value of creatinine increased significantly in the positive control group (group 2) compared with negative control group (1.166±.150 vs. .6167±.248mg/dL respectively). Other treated groups showed a significant decrease in creatinine compared with positive control group.

Table (6): The effect of date palm pollen and royal jelly on liver enzymes and creatinine of rats with testicular injury induced by sodium valproate

Groups	AST (IU/L)	ALT (IU/L)	Creatinine (mg/dL)
	Mean ± SD	Mean ± SD	Mean ± SD
Group (1)	51.83± 1.94^{d}	35.83± 3.18^{c}	.6167± .248^{c}
Group (2)	65.50± 2.88^{a}	53.50± 2.88^{a}	1.166±.150^{a}
Group (3)	59.16± 5.27^{b}	43.00±2.68^{b}	.8167± .075^{b}
Group (4)	56.50± 1.64^{cb}	43.83± 2.63^{b}	.783±.116^{cb}
Group (5)	55.00± 1.41^{dc}	41.16± 1.169^{b}	.816±.075^{b}

Data are presented as mean±SD. Values with different letters indicate significant differences among groups at $p \leq 0.05$

Histopathology examination results:

The present work was carried out to study the effect of date palm pollen and royal jelly on rats with testicular damage induced by sodium valproate.

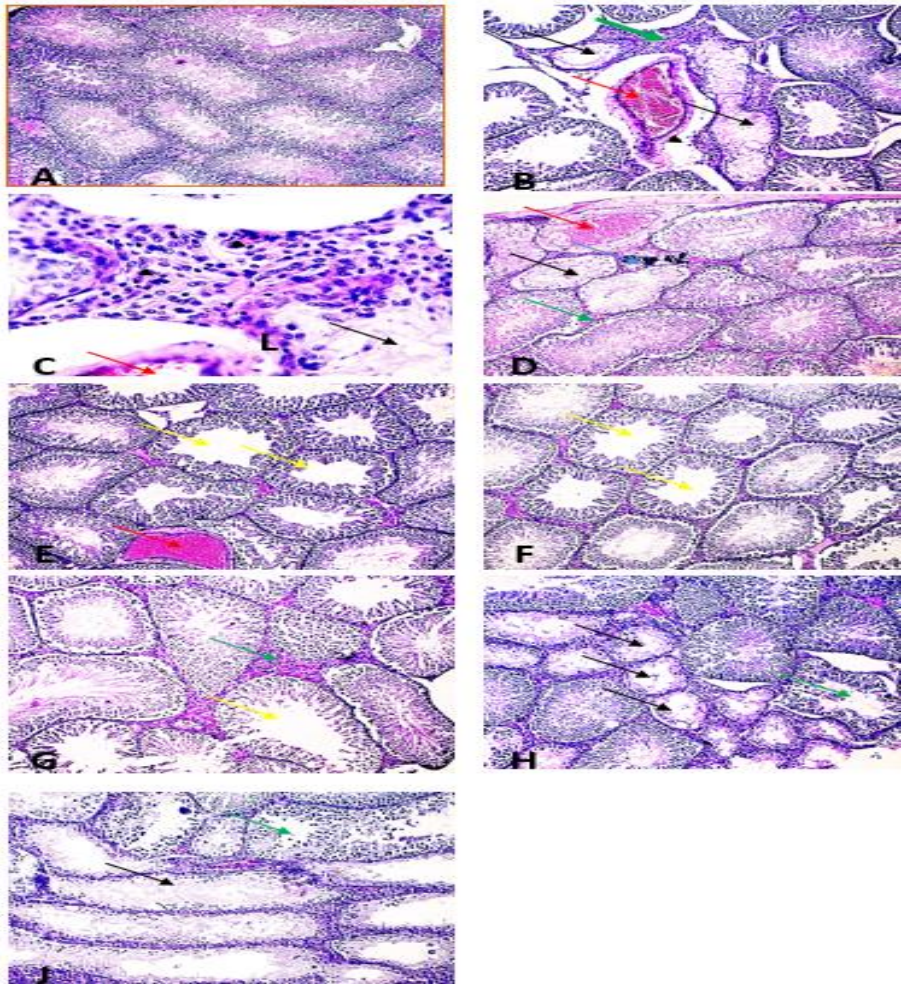

Fig. 1: Microscopic pictures of H&E stained testicular sections showing normally organized transversely cut seminiferous tubules lined with several layers of rounded spermatogonia and spematocytes along with Sertoli cells with minimal interstitial tissue in control negative group 1 (A). Necrotic tubules (black arrows), congested blood vessel (red arrow) with increased amount of interstitial tissue (white arrow) (B) infiltrated with mononuclear cells (arrowheads) (B&C), necrotic tubules (black arrows), congested blood vessel (red arrow) and dystrophic calcification (blue arrow) (D) are seen in untreated diseased group 2. Congested blood vessel (red arrow) and some dilated transversely cut seminiferous tubules showing widened lumen free of sperms (yellow arrows) are seen in diseased group treated with Viagra 3(E). Some transversely cut seminiferous tubules showing widened lumen free of sperms (yellow arrows) (F) with increased amount of interstitial tissue (white arrow) (G) in diseased group treated with palm 4. However, treatment using honey 5 doesn't evoke a protective effect as testicular sections in this group shows tubular degeneration (green arrows) and necrosis (black arrows) in transversely (H) and longitudinally (J) cut seminiferous tubules. X: 100 bar 100 except (C) X: 400 bar 50

Discussion:

Several studies studying the side effects of AEDs on male epilepsy patients have found that certain AEDs in epilepsy patients may induce reproductive and sexual disorders.**(Zhao et al., 2018).** Our results showed that there were significant decrease in weight gain , SOD, CAT, sperm count, sperm motility, sperm viability, testes hermon's (FSH, LH and testesteron), vesicle weight prostate weight and tests weight and significant increase in ALT, AST, creatinine, MDA and sperm abnormality, these results in agreement with **(Vijay *et al.*, 2008), (Girish *et al.*, 2014),** (**Zhao *et al.*, 2018) and (Mohamed *et al.*, 2019).Zhao *et al.*, (2018)** indicates that VPA may lead to a significant decrease in the levels of FSH and testosterone and alter the concentrations of LH, which might contribute to the reproductive endocrine dysfunction in male patients with epilepsy. After treatment with VPA, an increased production of GABA (a neurotransmitter that inhibits impulses between nerve cells in the brain) could cause negative

input from LH and FSH, leading their levels to decrease in male epilepsy patients. On the other hand, the GABA neurons can regulate noradrenaline directly to modulate the serum levels of LH and FSH and alter the balance of hypothalamic-pituitary-testicular (HPT) axis, leading to a decrease in the serum levels of these two sex hormones. LH, which is released by the pituitary gland, binds to the LH receptors on Leydig cells and activates adenylate cyclase to promote the biosynthesis of testosterone; FSH binds to the FSH receptors in Sertoli cells and forms androgen-binding protein, which can then combine with testosterone in the seminiferous tubules to drive the production of spermatozoa. Testosterone is the most important androgen in males; it plays crucial roles not only in supporting the function of prostate gland and seminal vesicles but also in the maintenance of different aspects of sexuality and sexual desire. Testosterone produced from Leydig cells and the decline in the level of LH decrease it. Thus, any reduction in the serum levels of LH, FSH, and testosterone will also impair both spermatogenesis and sperm aturation, as well as inducing testicular atrophy and disrupting other facets of male sexuality, such as libido and erectile function. A significant reduction in luteinizing hormones and follicle-stimulating hormones have been found. There was a substantial decline in sperm parameters for all measured elements (sperm motility, count and morphology) **(Mohamed et al, 2019)**.Also **Girish *et al,* (2014)** concluded that the weight, weight of the testis, sperm count and sperm motility in sodium valproate treated group (400 mg/kg) was significantly decreased and caused sperm abnormalities in male Wistar rats. Also The histopathological examination revealed that sodium valproate had caused degeneration and desquamation of germinal cells in the epithelium and also showed a decrease in the Johnsen's scoring , necrosis (thick arrow) and (thin arrow) and edema (broken arrow). **Vijay *et al,* (2008)** found that Valproate causes reversible change in intratesticular testosterone and LDH.

Also our results revealed that RJ, DPP and viagra treated rats showed significant increase in weight gain , SOD, CAT, sperm count, sperm motility, sperm viability, testes hermon's (FSH, LH and testesteron), vesicle weight prostate weight and tests weight and also showed significant decrease in ALT, AST, creatinine, MDA and sperm abnormality compared with valproate treated rats. These results in

agreement with **(Hess *et al,* 1997), (Miura *et al*, 2003), (Nayernia *et al*, 2004), (Marah *et al,* 2005), (Bahmanpour *et al.*, 2006), (Ghanbari *et al.*, 2015),** (**Azad *et al.*, 2018**) and (**Ebadimanas, 2018).**

Marah et *al.*, (2005) determined the possible therapeutic effects of date palm pollen in male infertility and concluded that the treatment by date palm pollen significantly increased serum LH, FSH, testosterone levels, sperm count and motility. Also **Bahmanpour *et al.*, (2006)** revealed to the consumption of DPP suspensions improved the sperm count, motility, morphology and indicated that date palm contain estradiol and flavonoid components that have positive effects on the sperm quality. The scavenging properties of DPP is the main important effects on the sperm parameters. Our results confirmed that DPP had beneficial effects on male reproductive activity. The DPP concentrations up to 120 mg/kg showed the best effects on sperm parameters. Our data showed an increase in the weight of testis and seminal vesicle in the rats that consumed DPP suspension. This effect might be due to the presence of gonadotropin like substances or steroidal component present in the DPP **(Nayernia *et al.*, 2004) and (Miura *et al.*, 2003).** Our data showed that using DPP suspension increases the plasma level of testosterone. The weight gains observed in epididymis, testes and seminal vesicles, in this study might have been due to fluid resorption effects of estradiol, which improved fertility. This might be due to the presence of phytoestrogen, as a steroidal component of DPP, which may have influenced sperm parameters **(Hess *et al.*, 1997).**

Azad et *al.*, (2018) showed that royal jelly reduced reproductive toxicity of nicotine in mice by improving the testicular structure and sperm parameters. **Ebadimanas, (2018)** found that royal jelly has protective effects on the DNA maturity of sperms and early in vitro embryonic development in ofloxacin treated rats. (RJ) improved reproductive parameters such as testicular weight, sperm count, viability, motility, deformity, DNA integrity, chromatin quality, serum testosterone and testicular tissue MDA levels in diabetic rats according to **(Ghanbari *et al.*, 2015).**

Treatment with RJ significantly improved sperm motility, count, and likeability, which might be mediated through its reputable antioxidant

lead to activity that remarkably protects sperms against oxidative damage. RJ has anti-inflammatory properties and an inhibitory effect on the release of pro-inflammatory cytokines**,** which might be related to its component of trans-10-hydroxy-2-decenoic acid, 10-hydroxydecanoic acid, and sebacic acid. treatment with RJ significantly ameliorated the hormonal imbalance and this may be attributed to its antioxidant properties that was derived from the short-chain peptides, phenolic compounds (flavonoids and cinnamic acid derivatives), some vitamins (A, E, and C), minerals (Fe, Zn, and Cu), and fatty acids (trans-10-hydroxy-2-decenoic acid) in the rebalancing of oxidant-antioxidant status as reflected on the MDA and GSH concentrations and CAT activity in testicular tissues (**Tohamy *et al.*, 2019).**

Conclusion :

In the present investigation, treatment with royal jelly and date palm pollen has effectively alleviated most against sodium valproate induced testicular toxicity and oxidative stress in male rats. Effects role of royal jelly and date palm pollen attributed to increased testosterone and enhanced activity of antioxidant enzymes. The study suggests that intake of royal jelly and date palm pollen may be beneficial for male patients suffering from low fertility due to oxidative stress.

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