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REPRODUCTIVE PERFORMANCE IN RATS AND EWES TREATED WITH PYRETHROID (ECTOMIN)

(With 5 Tables & 7 Figures)

By

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الكفاءه التناسليه فى الفئران والنعاج المعالجه بمادة البيروثرويد (الآكتومين)

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أستهدفت هذه الدراسه أستيضاح أثر الاكتومين كمثال للبيروثرويد فى ذكور وأناث الفئران البيضاء كنموذج لحيوانات التجارب وأيضاً على النعاج كنموذج لحيوانات المزرعه. أستخدمت فى هذه الدراسه خمس وعشرون من ذكور الفئران البالغه لدراسة مدى التأثير على خصوبة الذكور وأعطيت هذه المجموعه مادة الاكتوميين بجرعه ٣١ مجم / كجم لمدة ستون يوماً تم ذبح هذه الحيوانات كل ١٥ يوماً وقد أظهر الفحص وجود نقص معنوى فى أوزان كلا من الخصى والحويصلات المنويه وغدة البروستاتا وقد أظهر الفحص وجود نقص معنوى فى كلا من الحركه المتقدمه وفى نسبة الحيوانات المنويه الحيه وفى تركيزها بالاضافه الى وجود زياده معنويه فى نسبة الحيوانات المنويه المشوهه وقد أظهرت الدراسات الهستولوجيه وجود اضطراب وظيفى فى الخصيه وذلك نتيجة لوجود تحلل فى الخلايا المكونه للمنى وأنفصال للخلايا الميته وتقشر الخلايا السليمه بالاضافه إلى تكسير واضح فى الخلايا البينيه. أستخدمت فى هذه الدراسه أربعون من أناث الفئران البالغه لاجراء الدراسه المتعلقه بتشوهات الاجنه وقد أعطيت الفئران مادة الاكتومين من اليوم السادس إلى الخامس عشر من فترة الحمل (فترة تخليق الاعضاء). ١. فحص الشكل الخارجى أظهر وجود أنغراس جنينى ، أجنه ممتصه بالاضافه إلى وجود نقص معنوى فى متوسط وزن الأجنه الحيه ٢. فحص الحشاء أظهر وجود تضخم فى عضلة القلب ، أتساع فى الحوض الكلوى بالاضافه إلى قلة النمو النسيجى للرئتين ٣. فحص الهيكل العظمى أظهر وجود تعظم غير كامل للجمجمه ، بالاضافه إلى غياب عظم القص. أستخدمت فى هذه الدراسه عشرة نعاج لاجراء الدراسات الهرمونيه وقد تم رش هذه النعاج بمحلول الاكتومين بتركيز ١: ٥٠٠ أثناء اليوم الأول من ظهور الشبق وتم رش الحيوانات مره ثانيه بعد ١٥ يوم وقد أظهرت النتائج أن دورة الشبق لم تتأثر من حيث الطول وتتابع وكذلك لوحظ وجود نقص

معنوى فى مستوى هرمون البروجيستيرون فى اليوم التاسع من الدوره الثانيه والثالثه وكذلك فى اليوم الثانى عشر لدورات الشبق الثلاثه بعد الرش . وكذلك لم يلاحظ أى فرق معنوى فى مستوى هرمون التبويض والهرمون الحاث للحويصلات.

SUMMARY

The present study aimed to study the reproductive effect of Ectomin as pyrethroid insecticide in albino female and male rats as a model of experimental animals and ewes as a model of farm animal. Twenty five male rats were used for male fertility. They were given Ectomin (31 mg/kg .b.wt) for 60 days. Animals were sacrificed every 15 days. Ectomin resulted in a significant decrease in weight of testis, seminal vesicles prostate gland. It also cause a significant decrease in all parameters of male fertility (progressive motility, live sperms and sperm concentration) in addition to significant increase in sperm abnormalities. Histological studies revealed that Ectomin induce testicular dysfunction by inducing clear signs of degenerative changes of the spermatogenic cells, detachment of necrotic cells, desquamation of normal intact spermatocyte and in addition to clear destruction of interstitial tissue. Forty mature albino female rats were used for teratological examination. They were given Ectomin on day 6-15 of gestation (the period of organogenesis). 1-The morphological examination revealed the presence of implantation sites, resorbed foetuses and the living foetuses showed decreased body weight. 2-The visceral examination revealed the presence of cardiomegaly, dilatation of the renal pelvis and hypoplasia of the lung. 3-The skeletal examination revealed the presence of incomplete ossification of the skull, large open fontanelle and absence of sternbrae. Ten ewes were used for hormonal profiles. Ewes were sprayed with Ectomin (1/ 500 in D.W) during the 1 st day of heat and second spraying was applied 15 days later. The present result revealed that spraying of Barki ewes by Ectomin had no impairment effect neither on the sequencing of estrous cycle nor its length. A significant decrease of P4 (progesterone) was observed on day 9 of estrous cycle (starting of peak level) in the 2nd and 3 rd estrous cycle, and on day 12 of the three estrous cycle followed spraying. On the other hand neither the pattern of gonadotrophins (FSH & LH) nor their levels was affected by Ectomin.

Keywords: Reproduction-Rats and ewes-Ectomin.

INTRODUCTION

The pyrethroids are a class of natural and synthetic organic compounds which have been used commercially for many years because of their well known insecticide properties. These agents are still highly effective and often included in many currently avalilable household sprays *(GOSSELIN et al, 1984).*

The synthetic pyrethroids are rapidly absorbed and distributed through body tissue, including the brain *(GOSSELIN et al., 1984).* The previous studies about the neurotoxicity of the pyrethroids have indicated interaction of these compounds with the gamma amino butyric acid (GABA) receptors and other C..N.S. stero-specific receptors; the calmodulin - phosphodiesterase system and sodium channels in the mammalian brain *(LAWRENCE and CASIDA 1983., RASHATAWER and MATSUMURA, 1985 and SODERLUND).*

The natural pyrethroid had a teratogenic effect on the genital tract of the birds *(LUTZ-OSTERTAGE and LUTZ., 1974)* and may had antiandrogenic properties *(BRODY et al., 1983).* Haematological and enzymatic change had been reported in rabbits *(HASSAN et al., 1993)* rats *(FAKHRY et al., 1990)* and mice *(IBRAHIM et al., 1991)* exposed to aerosols of the pyrethroid inseticide (Ezalo).

The purpose of this study is to evaluate the teratogenic and spermatogenic effect in rats of one of commonly used pyrethroid compound (Ectomin) in Egypt as well as its effect on estrous cyclicity and hormonal profil of Barki ewes.

MATERIALS and METHODS

I - *Effect of Ectomin upon Albino rats:*

Sexually active albino rats of 150-200 gm weight and 4-6 months old, were divided into 2 groups:

Group 1: Twenty five adult mature male rats were sued to study the effect of oral administration of 1/10th of LD 50 (31 mg/Kg. b.wt) of Ectomin on male fertility and histological examination.

Group 2: Forty mature albino female rats were used to study the effect of oral administration 1/10th of LD 50 (31 mg/Kg. b.wt) for studying the teratogenic effect. These animals were kept under same conditions and fed upon a balanced ration.

1- Male Fertility:

Administration of Ectomin (1/10th of LD 50) was carried out for 60 days because the lenght of the complete spermatogenic cycle is about 48 to 52 days in the rat *(CLERMENT and HARVEY 1965)*. Animals sacrificed every 15 days for spermatozoal examination. Spermatozoa were obtained by maceration of the epididymis and vas deferentia and examined for progressive motility, live and dead sperms and concentration of sperm cells, using the technique described by *BEARDEN and FLUQUARY (1980)*. Testes and sexual accessory glands were taken out, weighted and subjected to histological examination.

2- Histological examination:

Testes were collected directly after slaughter and fixed in Bouin's fluid *(BOWIN, 1987)*. The fixed specimens were routinely processed and embedded in paraffine wax, sectioned and stained with Haematoxylin and Eosin stain *(HARRIS, 1900)* and periodic Acid Schiff's (PAS) *(PEARSE, 1985)*.

3- Teratogenic examination:

of Administration of Ectomin (1/10th LD50) was carried out at the 6th to 15th day gestation period, where these time is considered the period of organogenesis during which the organs are more sensitive to the effects of the toxic substances *(SNELL, 1982)*. Both treated and control pregnant female groups were kept under observation until the 20th day gestation then dams were killed by diethyl ether and the foetuses were examined by morphological, skeletal and visceral examination using the technique described by *HAYES (1986)*.

II- Effect of Ectomin on Barki ewes:

Ten apparantly healthy mature Barki ewes were used to investigate the effect of Ectomin on hormonal profile. In addition to ten ewes were as a control group (not subjected to spraying).

1- Oestrus synchronization:

Oestrus synchronization performed using veramix (up John Flemingway Sussex) The sponges are removed after thirteen days, and ewes were subjected to spray of Ectomin 1/500 in D.W., then during the following 3-5 days the animals come in estrous and this was detected by using vasoctomized ram. The day on which the ram marked the female was considered the 0 day. The spraying was repeated again after 15 days.

2- Separation of serum samples:

Blood samples were collected daily for estimation of FSH and LH allover the oestrous cycle and two times per week for progesterone determination. Serum was separated and kept at -20 °C until hormones assay.

RESULTS

1 - Effect of Ectomin upon male fertility:

a- Effect of Ectomin upon male sex organs:

Administration of Ectomin for 60 successive days reulted in statistically significant decrease in the weight of the testis and prostate gland, in addition to, significant increase in weight of seminal vesicles ($P < 0.05$) in comparison with the control group (table 1).

b- Effect of Ectmin upon spermatozoa:

Administration of Ectomin for 60 successive days resulted in statistically significant decrease in the percent of live sperms, this decrease was marked only at 60 days of experiment where the value being (48.4 ± 3.34) while in the control group being ($78 \pm 3.38\%$) (table 1) and there was a significant decrease ($P < 0.05$) in cocentration of sperms allover the experimental period, where the values being (89 ± 3.09, 87 ± 1.04, 176 ± 5.33 and 122.2 ± 114 /106,) in comparison to control groups (table 2) in addition to significant increase in the percent of spermatozoal abnormalities (Table 2).

2 - Histopathological finding:

Histopathological examination of the testis of control group showed normal structure with active spermatogenesis. The seminiferous epithelium had various stages of spermatogenesis (Fig. 1-a). The interstitial tissuse contained active leydig cells with fine periodic acid shiffe's (PAS) positive granules and vacuolated cytoplasm (Fig. 1-b). Administration of Ectomin resulted in marked degenerative necrotic changes in the epithelial lining of the seminiferous epithelium which was not detected in control group.

In group I : (given 31 mg/Kg b.wt. for 15 days) degenerative changes appeared in the form of granulation of the apical half 0 seminiferous epithelium fragmentation of intratubular sperm and pyknosis, Karyorrhexis and Karyolysis of some of nuclei of the spermatogenic cells, (Fig.2).

In group II : (given 31 mg /Kg. b.wt. for 30 days) these degenerative changes were advanced so the majority of germ cells had disappeared and the few cells left were pyknotic or lysed. The degenerated and necrotic cells appeared detached in the lumen with darkly stained nucleus and acidophilic cyloplasm (The detachment of necrotic cells were accompanied by vacuolation of seminiferous epithelium which were frequently seen near the basement membrane and occasionally seen in the thickness of the epithelium (Fig. 3).

In group III : (given 31 mg /Kg. b.wt. for 45 days) the spermatids were almost absent from many tubules and desquamation of normal intact spermatocyte into the lumen, which were accompanied by epithelial disorganization or missing of group of cells from the seminiferous tubules.

In group IV : (given 31 mg /Kg. b.wt for 60 days) The seminiferous tubules showed the same lesions as in the previous groups but more tubles appeared to be affected and showed various degrees of cellular loss among their layers mainly in the layers of young spermatids.

The interstitial tissue showed clear destruction and the tubules were widely separated from each other and leydig cell had no vacuoles in its cytoplasm (inactive).

3 - Teratological examination:

The teratological examination of the foetuses obtained from treated dams carried out by morphological, visceral and skeletal examination.

a- External morphological examination:

The morpholoical examination of the foetuses revealed the presence of the implantation sites at a higher precentage (33.3%) than those of the control group (zero). The resorbed foetuses was recorded as 11.1% the viable foetuses showed less values (33.33%) than that of the control group (89.28%). The living foetuses showed decreased body weight, the mean value of body weight were 20.83 $\pm$ 0.143 gm in the treated group, compared with 3.89 + 0.17 gm in control group (table 3) Dwarf foetuses were observed in (2.33%) of the foetuses.

b- Visceral examination:

The visceral examination of the foetuses revealed the presence of :-

Cardiomegaly was noted in a percentage of 21.42, dilatation of renal pelvis was noted in a percentage of 14.28 and hypoplasia of the lung was noted in a percentage of 7.41 (table 4).

c- Skeletal examination:

Skeletal examination of the foetuses revealed the presence of incomplete ossification of the skull and large open fontanelle was recorded in a percentage of 30.76 of the foetuses. Absence of sternbrea were noted in a percentage of 38.46. Absence of the phalanges in the fore and hind limbs in a percentage of 34.62. Absence of caudal vertebrale was noted in 23.07% of the foetuses Absence of metacarpal bones was noted in a percentage of 23% (table 5).

II- Effect of Ectomin on estrous cycle and hormonal level of Barki ewes:-

The present results reveald that spraying of Barki ewes by Ectomin had no impairment effect neither in the sequencing of estrous cycle nor on its length. A significant decrease of P4 was observed after Ectomin treatment on day 9 of estrous cycle starting of peak level as a represented to the ovarian activity. The P4 concentration were 3.19 $\pm$ 0.29, 2.67 $\pm$ 0.21 and 2.56 $\pm$ 0.17 mg ml serum on the 1st, 2nd and 3rd estrous cycles respectively after

Ectomin treatment, rather than 3.83 ± 0.14 mg / ml serum in the control. There is also a significant decrease in P4 levels at days 12 in the three estrous cycles, followed Ectomin treatment (4.45 ± 0.04, 3.99 ± 0.33 and 3.54 ± 0.32 mg/ ml) (Fig : 5). On the other hand, spraying of Ectomin had no significant influence neither in the pattern nor in the levels of FSH or LH during the three estrous cycle after treatment. (Fig : 6&7).

DISCUSSION

I - Effect of Ectomin upon Albino rats:-

1 - Effect of Ectomin upon Male Fertility:

Oral administration of Ectomin cause significant decrease in the weight of sexual organs, sperm count and progressive motility. Also significant increase in the percentage of sperm abnormalities. Similar finding were recorded by *EL-ASHMAWY et al., (1993) and SOBHY (1991).* The inhibitory effect of pyrethroid in the male reproductive organs and spermatozoal picture may be attributed to the significant decrease in L H, FSH and testosterone levels as have been mentioned by *EL-ASHMAWY et al., (1993)* or may be attributed to the direct cytotoxic effect of pyrethroid on the tissue of the testis. This opinion was proved by the histopathological degenerative changes in the testis.

The reduction in the sperm concentration could be attributed to reduction in the meiotic index of the testicular cells which might be due to the usage of the pyrethroid access the blood testis barrier (BTB) and gain access to the germ cells in seminiferous tubules. *DIXON and LEE (1973)* reported that the BTB appeared to represent an important aspect in the consideration of reproductive and mutagenic effects of environmental chemicals. *OKUMURA et al (1975)* recorded that the permeability characteristics for the BTB are generally similar to those limit penetration of membranes of the central nervous system. Pyrethroids distributed through the brain and the principle action of them is the nervous system *(GOSSELIN et al., 1984 and KUMAR, 1984).*

2 - Histopathological findings:

In the present study it was found that pyrethroid (Ectomin) may induce testicular dysfunction by inducing clear signs of degenerative changes affecting spermatogenic cells, detachment of necrotic cells and desquamation of normal intact spermatocyte.

The degenerative changes affecting spermatogenic cells appeared in the form of pyknosis, karyorrhexis and karyolyses. These results were in accordance with *SOBHY, (1991) and HASSAN et al. (1993)* who reported that pyrethroid cause severe degenerative changes in the seminiferous

tubules, so the tubules are lined by a layer of Sertoli cells, then the degeneration increase to cause severe hypoplasia and complete necrosis. This degeneration may be due to fluctuation in the level of FSH which has a direct effect upon the germinal epithelium and Sertoli cells which are responsible for development of spermatozoa *(HASSAN et al., 1993)*. In the present study the degenerated and necrotic spermatogenic cells appeared detached in the lumen. These results were in accordance with *(SOBHY, 1991 and HASSAN et al., 1993)* who found multinucleated giant cells detached in the lumen which may be formed as a result of fusion of degenerated spermatogenic cells.

The clear desquamation of normal intact spermatocyte in the lumen observed in the testis subjected to different toxic chemicals or may be responsible for persistent decrease in FSH level as have been mentioned by *SUN et al. (1990)*. The detachment of degenerated cells in addition to desquamation of intact spermatocyte may lead to epithelial disorganization and missing of seminiferous epithelium. This may be due to inhibition of microtubule formation in Sertoli and mitotic division of germ cells as previously seen with single doses of other microtubule poisons *(RUSSELL et al., 1981)* or direct effect of toxicants on Sertoli cell function *(HESS et al., 1991)*.

In the present study the pyrethroid (Ectomin) induced impairment of androgen synthesis through its direct effect upon leydig cells which had no PAS +ve granules or cytoplasmic vacuoles. Our results are in accordance with *SOBHY (1991) and HASSAN et al (1993)* who found that interstitial tissue is oedematous with clear proliferation of fibrous connective tissue. The direct effect upon Leydig cell may be due to fluctuations in the level of LH which stimulates testosterone secretion by the leydig cells.

3 - Teratological examination:-

The most common teratogenic effect of pyrethroid were decrease in the percentage of survival foetuses, increased number of resorbed foetuses and reduction in the foetal weight. Similar finding were mentioned by *SOBHY (1991) and ABDEL-KHALIK et al. (1993)* who mentioned that pyrethroid cause significant decrease in the number of corpora lutea and implantation sites and cause early resorbition of foetuses. The visceral and skeletal examinations showed hypoplasia of the lung, dilatation of the renal pelvis, hypertrophy of the heart, incomplete ossification of the skull and absence of some sternbrae, reduction in the number of caudal vertebrae and absence of some phalanges. Similar finding were mentioned by *HANAFY et al. (1986)*.

II- Effect of Ectomin on oestrous cycle and hormonal level of Barki ewes:-

The present result revealed that spraying of ewes (two times daily for 15 days interval) with Ectomin, had no deleterious effect neither on estrous cycle sequencing nor the length. This result is in agreement with the previous study reported by *ABD EL-DAIN (1993)* in buffalo. On the other hand, cyclic pattern of P4 was not affected by Ectomin treatment and similar to that described by *THORBURN et al., (1969). and ELIAS (1987)* for the normal ewes. The insignificane ($P < 0.01$) of P4 concentration on the 1st estrous cycle followed spraying is in agreement with *SHALABY (1989)* in the first days of pregnancy of ewes and may reflect the slow absorption of Ectomin through skin. However, the significant decrease of the P4 peak on day (9-12) in the second and the thrid cycles followed Ectomin treatment may be due to absorption of this insecticide either through mucous membrane, skin abrasion or may be through intact skin, this is in agreement with *SHALABY (1989)* who found slight decrease in P4 later on during pregnancy of ewes.

On the other hand neither the pattern of gonadotrophins (FSH & LH) nor their levels was affected by *ECTOMIN.* The absence of any effect on these hormones in the three cycles may be due to the short half life of LH and FSH in ovine serum *(ELIAS, 1991)* which may not allow any accidental effect of insecticides, In contrarly with progesterone which was present during almost the days of oestrous cycle except around heat time *(ELIAS, 1987)* This insignificant changes in level of both L hand F.S.H. hormones in ewes may be attributed to the minor or no effect of Ectomin on hypothalamic nuclei concerned with reproductive control. This opinion was supported by short time of application and smaller dosage used (Therapeutic doses).

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Table (1): Mean values of sexual organs weights

Parameters		Control (n = 5)	Ectomin (n = 5
15 days	testes weight/g	1.27 ± 0.083 b	1.33 ± 0.025
	prostate gland weight/g	0.222 ± 0.038 c	0.69 ± 0.023 b
	seminal vesicle weight/g	1.117 ± 0.094 b	1.31 ± 0.066 b
30	testes	1.36 ± 0.024 b	1.19 ± 0.082 b
	prostate gland weight/g	0.432 ± 0.068 b	0.34 ± 0.011 b
	Seminal vesicle	1.106 ± 0.0411 b	0.342 ± 0.018 c
45	testes	1.58 ± 0.061 a	1.25 ± 0.104 b
	prostate gland weight/g	0.76 ± 0.063	0.556 ± 0.138
	seminal vesicle	1.22 ± 0.10 b	1.78 ± 0.107 c
60	testes weight/g	1.27 ± 0.053 b	1.38 ± 0.029 b
	prostate gland weight/g	0.98 ± 0.195	0.608 ± 0.117
	seminal vesicle weight/g	1 ± 0 b	1.742 ± 0.04 a

Table (2): Mean values of spermatozoal examination.

Parameters		Control (n = 5)	Ectomin (n = 5)
15 days	Progressive motility %	68.13 ± 6.59	61 ± 2.448
	Live sperm %	71 ± 1.87 b	79 ± 1.82 a
	abnormalities %	13.4 ± 1.80 a	9.4 ± 1.122 b
	sperm concentration 10^6/ml	148.6 ± 2.99 a	89 ± 3.09 b
30	Progressive motility %	67 ± 1.99 b	40 ± 3.53 c
	Live sperm %	73.8 ± 2.65	69.4 ± 3.78
	abnormalities %	14 ± 2.915 a	8.7 ± 7.44 a
	sperm concentration 10^6/ml	111.2 ± 2.43 b	87 ± 1.04 c
45	Progressive motility %	59 ± 2.915 b	53 ± 2.54 b
	Live sperm %	66.2 ± 4.114	66.4 ± 2.72
	abnormalities %	12 ± 2.54 b	25 ± 4.39 b
	sperm concentration 10^6/ml	169.8 ± 1.2 b	176 ± 5.33 c
60	Progressive motility %	47 ± 4.84 b	44 ± 2.54 b
	Live sperm %	56.8 ± 3.77 b	48.4 ± 3.24 b
	abnormalities %	27.4 ± 2.73 b	17.4 ± 2.08 c
	sperm concentration 10^6/ml	162.2 ± 2.53 b	122.2 ± 11.135 b

Table (3): Morphological examination of rat foetuses

Insecticides	Dose in mg/kg b.wt.	Total No. of dams	Total No. uterine implants	Implantation sites		Resorped foetuses		Living foetuses		Mean foetal weight/gm
				No.	%	No.	%	No.	%	No.
Control	0	10	56	0	0	0	0	50	89.28	3.87±0.17
Ectomin	8	10	63	21	33.3	7	11.1	21	33.33	2.83±0.14

Table (4): Visceral examination of rat foetuses.

Insecticide	Dose mg/kg b.wt.	No. of foetuses	Palate		Thymus		Heart		Lungs	
			No.	%	No.	%	No.	%	No.	%
Control	-	16	0	0	0	0	0	0	0	0
Ectomin	31	28	0	0	0	0	6	21.42	2	7.14

Table (5): Skeletal examination of rat foetuses .

Insecticide	Dose	No.	Malformations of							
	mg/kg b.wt	foetuses	Skull		Ribs		Sternum		Caudal vertebrae	
			No.	%	No.	%	No.	%	No.	%
Control	0	50	1	2	0	0	3	6	0	0
Ectomin	31	26	8	30.76	3	11.53	10	38.46	6	23.0

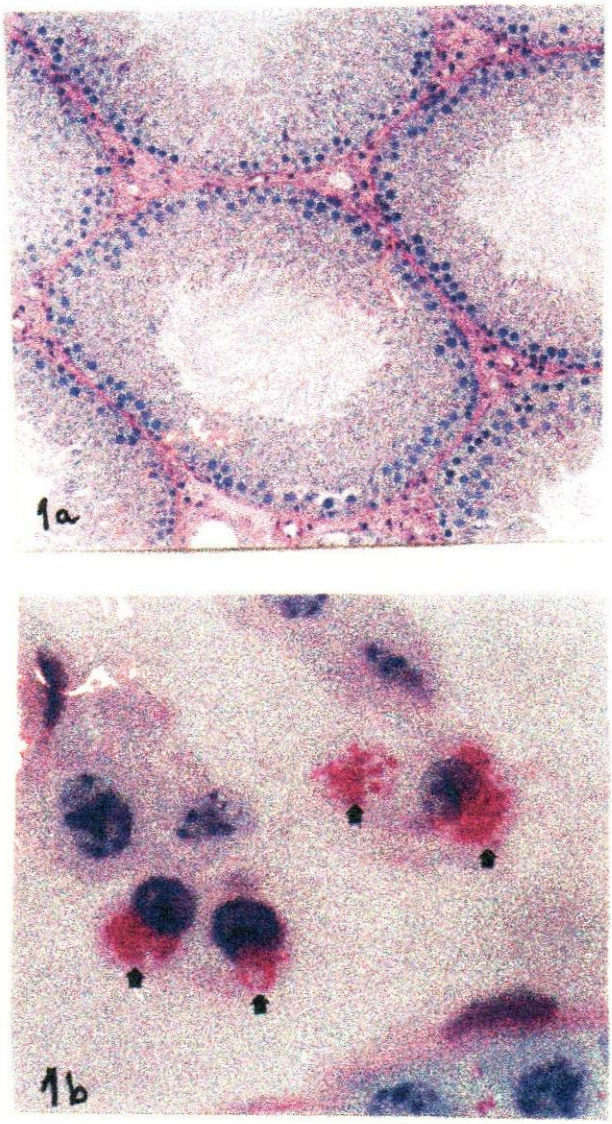


Fig. 1: Cross section in the testis of control rat showing:-
(1-a) normal seminiferous tubules with various stages of spermatogenesis.
stain: H&E X: 200
(1-b) normal interstitial cells with fine PAS positive granules
Stain: PAS X: 1000

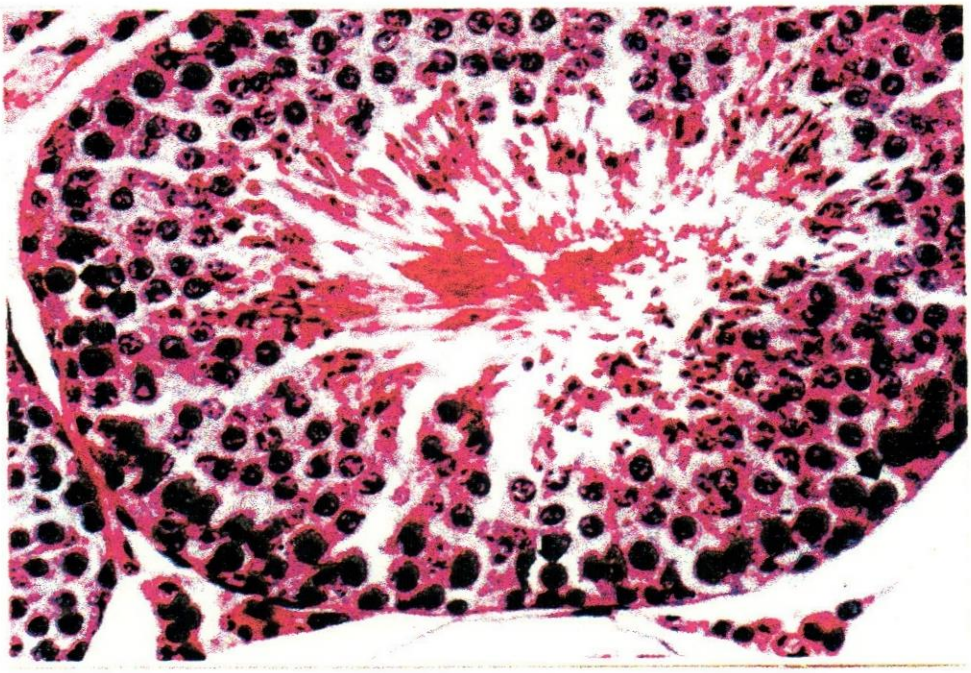


Fig. 2: Seminiferous tubules of rat in group II showing: degeneration appeared in the form of pyknosis and karyolysis.
Stain: H&E X: 400

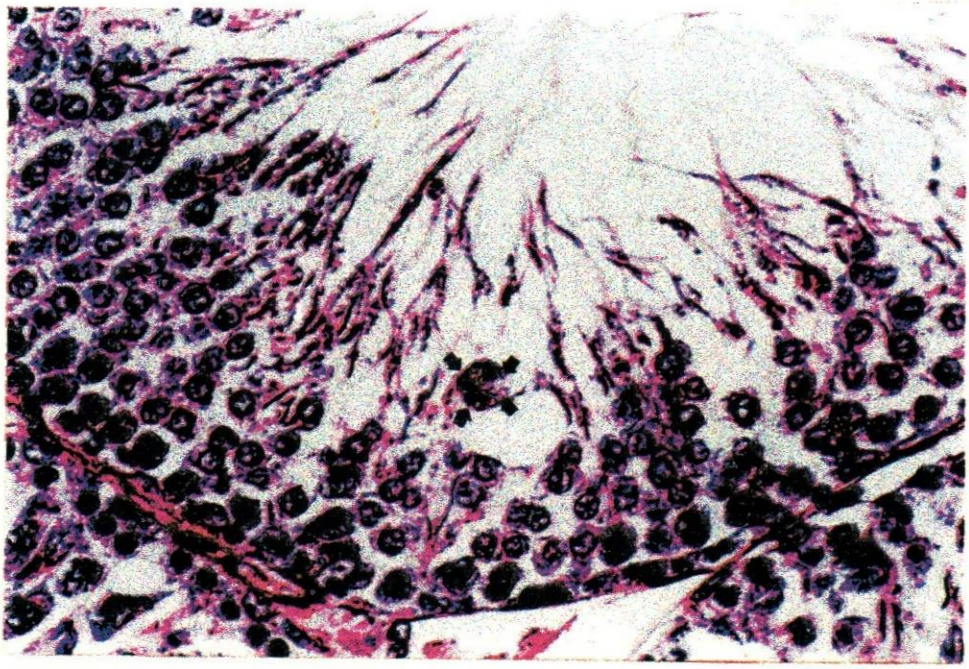


Fig. 3: Seminiferous tubules of rat in group II showing: degenerated cell with darkly stained nucleus and acidophilic cytoplasm slaughed in the lumen.
Stain: H&E X: 400

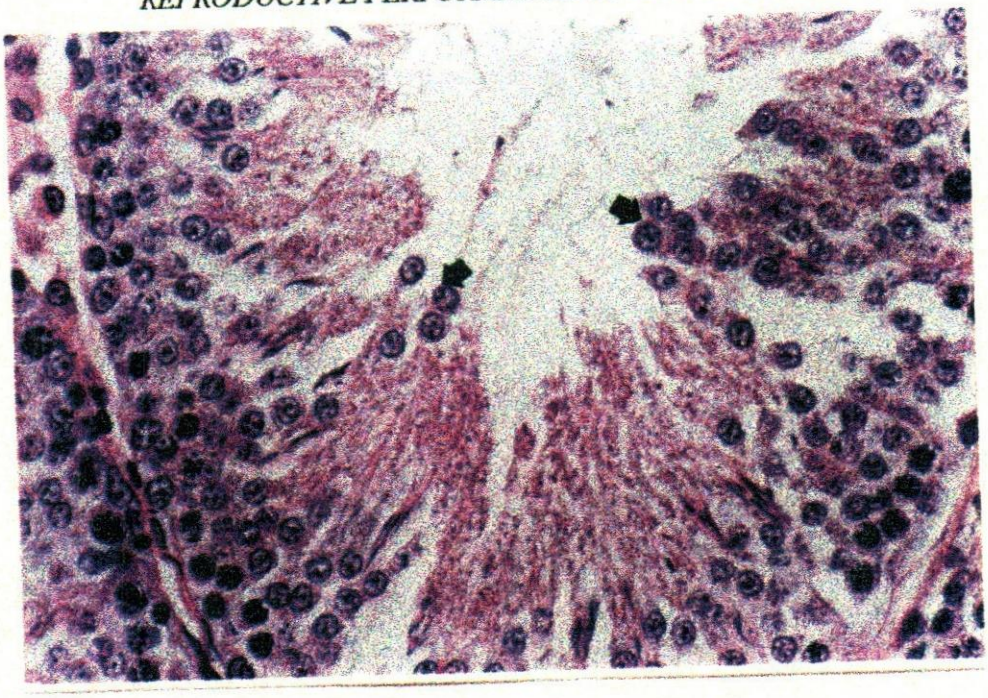
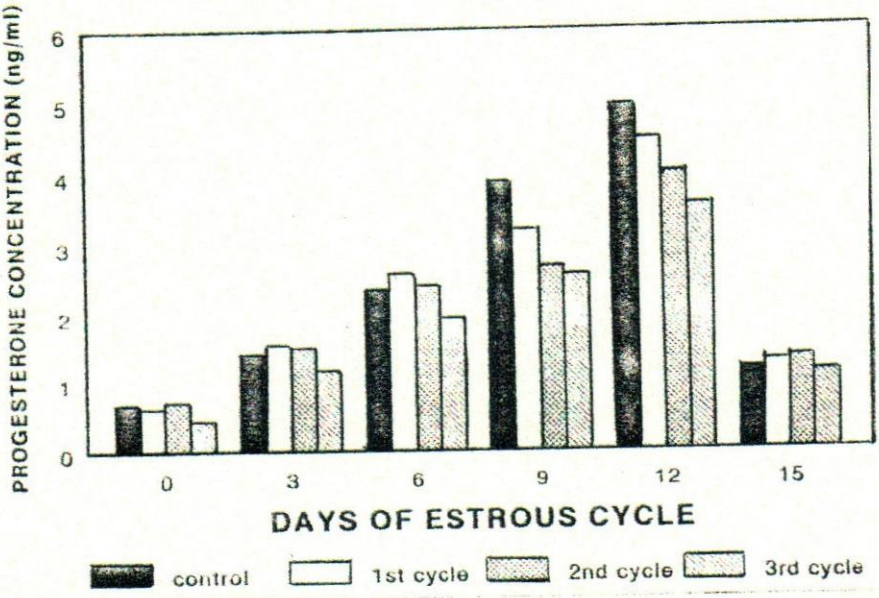


Fig. 4: Seminiferous tubles of rat in group IV showing: desqumation of the normal intact spermatocytes into the lumen.
Stain: H&E X: 40

FIG. (5) PROGESTERONE PROFILE DURING ESTROUS CYCLE IN RESPONSE TO ECTOMIN TREATMENT OF BARKI EWES



FIG(6): FSH PROFILE DURING ESTROUS CYCLE IN RESPONSE

TO ECTOMIN TREATMENT OF BARKI EWES

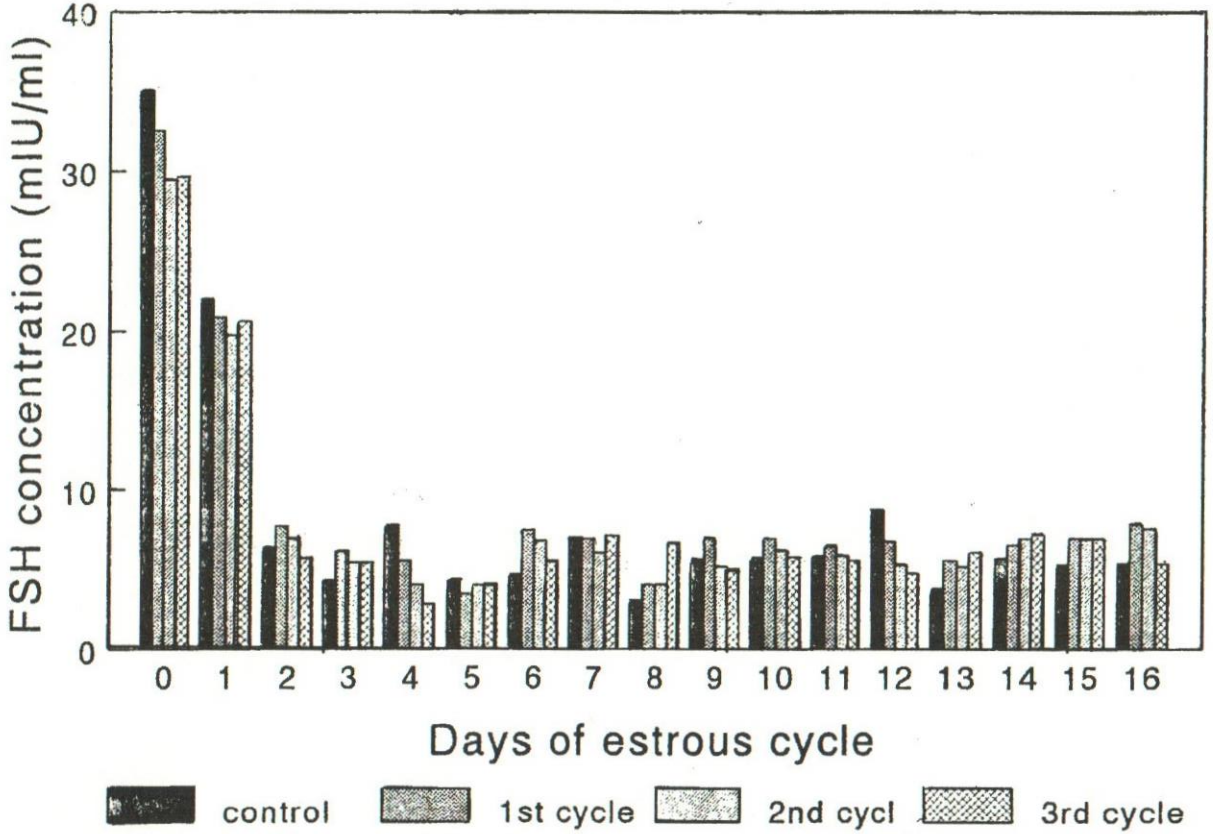


Fig.(7) LH PROFILE DURING ESTROUS BCYCLE IN RESPONSE TO ECTOMIN TREATMENT OF BARKI EWES